HerbalGram 94 • May-July 2012

Camu-Camu Profile • Post-fermented Tea Benefits • Chocolate & Heart Disease • Cannabis Update
Ginkgo Improves Cognition • Resveratrol Update • White Bean Extract & Weight Loss

HERBALGRAM

The Journal of the American Botanical Council

Number 94 | May - July 2012

Sausage Tree
Versatile African Herb

"Grapefruit Seed Extract" Adulteration

US/CAN $6.95

0 56698 81379 8 94

www.herbalgram.org

Sausage Tree: Versatile African Herb • "Grapefruit Seed Extract" Adulteration • Post-fermented Tea Benefits • Chocolate & Heart Disease • White Bean Extract & Weight Loss www.herbalgram.org

MISSION DRIVEN:

Educate & Inspire

Making Outstanding Extracts Has Never Been Enough.

Excellence in herbal extraction is at the heart of what we do. But the soul of Herb Pharm's mission is to lead people to embrace herbal healthcare by educating them on the safe and effective use of herbs, and inspiring a respect for plants and nature.

That means standing shoulder-to-shoulder with aspiring herbalists who attend our renowned **HerbaCulture Work-Study Program** to experience traditional cultivation and preparation of medicinal herbs.

It means that our organic farm is designated a **Botanical Sanctuary** by *United Plant Savers* in recognition of our work in the propagation and conservation of endangered medicinal plants.

It's seen in our higher education **scholarship fund**, which provides financial assistance to students of naturopathic medicine and clinical herbalism.

And it's why we offer **guided herb walks** and **educational seminars** to share our expertise with herbal enthusiasts and the herbally curious.

Educating, inspiring and offering outstanding herbal healthcare products, for more than 30 years that's been our secret formula.

For more information about Herb Pharm's educational programs visit us at www.herb-pharm.com/education.html or use your smart phone to scan the image to the left.

Camu-camu

Myrciaria dubia

Family: Myrtaceae

INTRODUCTION

Camu-camu, is a fruit-bearing shrub or small tree in the myrtle family (Myrtaceae) that grows around semi- to fully-flooded areas from Brazil to Peru, particularly around ox-bow lakes where there is not much current.[1-3] In Brazil, its geographical distribution ranges from the Atlantic coast in the state of Pará through the states of Roraima, Amazonas, Rondônia, and to the border with Peru.[4] It grows approximately 6-9 feet (2-3 meters) tall and has small white flowers. The plant produces green fruit 1 inch (2-3 cm) in diameter that turns reddish-purple as it ripens during flooding or high-water seasons.[1] The simple leaves are elongated with pointed tips and are from 1.5 to 4 inches (4-10 cm) long and 1 to 1.5 inches (2-4 cm) wide.[2] However, the variability in both leaf and fruit size can be much greater. For example, trees along the Putumayo River, an Amazon tributary which forms part of Colombia's border with Ecuador, were found to have leaves more than 2.75 inches (7 cm) wide and 5.5 inches (14 cm) long and fruits over 2 inches (4 cm) in diameter.[5]

Camu camu *Myrciaria dubia*. Photo ©2012 DirecTrade

In Peru, 2 different species are referred to as camu-camu. "Camu-camu arbustivo" (*Myrciaria dubia*) is widely distributed in the state of Loreto in the river basins of the Nanay, Napo, Ucayali, Marañon, Tiger, Tapíche, Yarapa, Tahuayo, Pintuyacu, Itaya, Ampiyacu, Maniti, Oroza, Putumayo, Yavari, and Curaray. "Camu-camu arbóreo" (*M. floribunda*) occurs throughout the southern part of the Peruvian Amazon in the state of Ucayali.[3,6] For the purposes of this article, only *M. dubia* will be discussed.

HISTORY AND CULTURAL SIGNIFICANCE

Myrciaria dubia (syn: *M. paraensis*, *Psidium dubium*) has numerous common names in addition to camu-camu, including *camo camo* (Peru); *araza de agua* (Spanish); *camu-camu negro* (Peru); *guapuro blanco* (Bolivia); rumberry (English); *cacari*, *azedinha*, *miraúba,* or *muraúba* (Brazil); *algracia*, *guayabillo blanco*, *guayabito*, and *limoncillo* (Venezuela).[5,7]

The fruit was first sold in Iquitos, Peru as one of a multitude of non-timber forest products (NTFPs) extracted from the wild, but until its promotion as an edible fruit in the 1970s, there was no significant international market for it as an NTFP.[5] There is very little published folklore on camu-camu as an edible fruit.[5] Rarely was the sour, acidic fruit eaten by the people of the rainforest and it has not been documented as a traditional herbal remedy for any condition in the Amazon region.[1] In Iquitos, the fruit recently has become popular in juice drinks, liqueurs, and ice cream.[1,3,8] Currently, in Peru, the juice is drunk straight or with water for flu, and stomach and intestinal conditions. Peruvians also make the bark into a poultice for wounds and take a bark decoction with fruit juice and rum for rheumatism.[8] Some Peruvians used it as fish bait and as a source of high-quality firewood.[4]

When its high vitamin C content was discovered, researchers and product developers in countries around the world became interested in the plant.[1] The vitamin C concentration of fresh camu-camu fruit averages 2.4 to 3.0 grams of ascorbic acid per 100 g of fresh pulp, which is roughly 30 times that of an orange.[1,3,5,8,9] Additionally, it provides 10 times more iron, 3 times more niacin, twice as much riboflavin, and 50% more phosphorus than oranges.[1] The fruits also provide 711 mg/kg of potassium, or 18 mEq (milliequivalents) of potassium per kg; the daily recommended amount is about 2,000 mg per day, or 51 mEq.[1,10] Beta-carotene, calcium, and thiamin are also found in the fruit, as is the anthocyanin, cyanidin 3-glucoside, and delphinidin 3-glucoside.[11,12]

Based on the vitamin C content, author and retired economic botanist, James A. Duke, PhD, suggests that the fruit may be used for aging, arthritis, asthma, cardioprotection, the common cold, Crohn's disease, eczema, flu, glaucoma, high blood pressure, high cholesterol, obesity, osteoporosis, pain, and Parkinson's, although research for most of these theoretical applications has not been conducted.[8]

CURRENT AUTHORIZED USES IN COSMETICS, FOODS, AND MEDICINES

In a February 2012 draft revision of the Codex Alimentarius Commission classification of foods and animal feeds, it is proposed that "Rumberry" (*Myrciaria dubia* (Kunth) McVaugh) be listed within commodity sub-group 005A "Assorted tropical and sub-tropical fruits – edible peel – small".[13] In the European Union (EU), camu-camu fruit and pulp are presently classified as "novel" foods with status "FS," meaning "According to information available to Member States competent authorities this product was used only as or in food supplements (FS) before 15 May 1997. Any other food uses of this product have to be authorised pursuant to the Novel Food Regulation."[14] As such, the oral use of camu-camu in the EU

Continued on page 2

presently is authorized only as a component of food supplement products,[15] for example as a source of vitamin C.[16] Through the World Trade Organization (WTO) process, the government of Peru is proposing that "traditional products" such as camu-camu that have a history of safe consumption in the country of origin and other parts of the world, barring the EU, be excluded from the scope of Regulation 258/97 of the European Parliament and of the Council concerning novel foods and novel food ingredients.[17]

Concerning the use of camu-camu in cosmetic products in the EU, the European Commission Health and Consumers Directorate lists both "Myrciaria Dubia Fruit Extract" and "Myrciaria Dubia Seed Extract" for use as a skin-conditioning (maintains the skin in good condition) ingredient. "Myrciaria Dubia Fruit Juice" (the juice expressed from the fruit) is listed for both antioxidant (inhibits reactions promoted by oxygen, thus avoiding oxidation and rancidity) and emollient (softens and smoothes the skin) functions.[18]

In North America, camu-camu is regulated as a component of notified dietary supplement products (source of vitamin C) in the United States.[19] In Canada, camu-camu is regulated as a component of licensed Natural Health Products (NHPs), for example as a medicinal ingredient of complex mixtures. These mixtures include ones in combination with acerola fruit (*Malpighia glabra*, Malpighiaceae) concentrate, bromelain (from pineapple, *Ananas comosus* or *A. bracteatus*, Bromeliaceae), citrus bioflavonoids, rose hips (*Rosa canina*, Rosaceae), rutin, and vitamin C for approved use a "a factor in the normal development and maintenance of bones, cartilage, teeth and gums,"[20] or, for example, in combination with Spanish black radish root (*Raphanus sativus* var. *niger*; Brassicaceae), and acerola fruit for an approved use as "an antioxidant for the maintenance of good health. Helps the body to metabolize fats and proteins."[21] As a non-medicinal ingredient (NMI), "Myrciaria dubia fruit flavour" is approved for use as a flavor enhancer component of NHPs.[22]

For the development of standards in Peru, a technical subcommittee for the standardization of camu-camu has been established within the membership of the *Instituto Peruano de Productos Naturales* (IPPN; Peruvian Institute of Natural Products).[23] In Brazil, a camu-camu research group was established in 1994 within the *Instituto Nacional de Pesquisas da Amazônia* (INPA; Brazilian National Institute of Amazonian Research). The research group, headed by Dr. Kaoru Yuyama, had over 20 scientific papers on camu-camu published in 2011 alone.[24]

MODERN RESEARCH

While there is research looking at the ecology, cultivation, pests (insects and fungi), and more on *M. dubia*, particularly led by the Instituto de Investigaciones de la Amazona Peruana (IIAP), there is very little clinical research on the plant. In a 2008 study evaluating the anti-oxidative and anti-inflammatory effects of camu-camu for the prevention of atherosclerosis in humans, 20 male smoking volunteers without other risk factors were randomly assigned to take 70 mL of 100% camu-camu juice (1050 mg of vitamin C) or 1050 mg of vitamin C tablets for 7 days.[12] There was an overall significant decrease in oxidative stress markers (urinary 8-hydroxy-deoxyguanosine, $p<0.01$; and total reactive oxygen species, $p<0.05$) and inflammatory markers (high sensitivity C reactive protein, $p<0.05$; interleukin-6, $p<0.05$; and interleukin-8, $p<0.01$) in the group taking camu-camu juice but no change in the vitamin C group. The source of this marked decrease in overall inflammation is thought to be due to not only the high concentration of vitamin C in camu-camu fruit, but also other antioxidant/anti-inflammatory components and/or substances that help increase the rate of absorption of vitamin C.

In a 2002 study evaluating the effects of camu-camu fruit extract with açaí (*Euterpe oleracea,* Arecaceae) fruit juice as sources of vitamin C and iron in preschoolers with mild anemia, 85 children (2 to 6 years old of both sexes) were randomly divided into 5 groups to take (once daily with lunch) 150 mL açaí juice (standardized to 2 mg iron), or 150 mL açaí juice (2 mg iron) with camu-camu extract (40 mg vitamin C), or iron amino acid chelate 1 mg, or iron amino acid chelate 2 mg, or deionized water for 120 days.[25] Regardless of the source of iron, no significant differences in hemoglobin concentrations were observed, although there was a better recovery of anemic children in the 2 mg iron amino acid chelate group. Significant weight gain was observed in both the açaí and açaí plus camu-camu groups.

The remainder of the literature on camu-camu is based on animal and pharmacological studies and the potential human uses of the fruit are extrapolated from this research. While these investigations are useful, it is clear that further clinical research is needed to evaluate any proposed medicinal uses.

A 2010 *in vitro* study compared the presence of bioactive compounds and the antioxidant/antidiabetic potential of 16 native Brazilian fruits and found that camu-camu had the highest antioxidant capacity, including the highest total phenolic and ellagic acid content, but did not inhibit alpha-amylase or alpha-glucosidase as efficiently as some of the other fruits.[26] Thus, it may not be as beneficial for the control of postprandial hyperglycemia as some of the other fruits studied.

A 2010 chemical study evaluated the changes in antioxidant capacity and total phenolic contents of camu-camu fruit at different stages of maturity.[27] In addition to the vitamin C content, camu-camu possesses 30 phenolic compounds including flavan-3-ols (catechin and its derivatives), ellagic acid derivatives, anthocyanins (delphinidin 3-glucoside and cyanidin 3-glucoside), flavonols (rutin and its derivatives), and flavanones (naringenin and eriodictyol derivatives), of which flavan-3-ols and ellagic acid were the most common at all stages of maturity. The presence of hydrolyzed tannins (gallo- and ellagitannins) was also shown.

In 2005, a chemical analysis also found that the major anthocyanins in camu-camu were cyanidin-3-glucoside (89.5%) and delphinidin-3-glucoside (4.2-5.1%).[28] This study examined the fruit from 2 different regions in Brazil and found that the region with higher rainfall and lower temperatures produced fruit with higher overall anthocyanin contents.

A chemical study in 2000 aimed to characterize the volatile compounds in a number of Brazilian fruits, in order to pave the way for finding ways to retain high-quality aroma and flavor in product production.[29] In this study, 21 different volatile compounds were found in camu-camu fruit, the majority of which were terpenes (98%), specifically alpha-pinene (66%) and *d*-limonene (24%).

Another 2000 study investigated the vitamin C stability in stored camu-camu and found an overall 23% decrease in vitamin C content after 28 days of storage, which remained relatively stable, increasing to only a 26% loss at 335 days of storage.[9] This represents a decrease in vitamin C from 2.4-3.0 g/100g of pulp to 1.57-1.21 g/100g of pulp.

FUTURE OUTLOOK

The principle forms of camu-camu exported from Peru are powder (73.40%), extract (10.44%), pulp (7.97%), dehydrated

Camu-camu *Myrciaria dubia*. Photo ©2012 DirecTrade

(4.72%), marmalade (1.72%), in capsules (1.13%), flour (0.01%), and other forms (0.61%). The reported customs value of camu-camu exports from Peru has declined significantly since 2007 with the 2011 export value (USD $922,103.56) at about one-fifth that of 2007 (USD $5,024,563.05). During the 13-year period of 1999 through 2011, calendar years 2006, 2007, and 2008 showed the highest export values for camu-camu.[30] The principle export markets for Peruvian camu-camu ingredients and products in 2008 were Japan (52.38%), the Netherlands (27.22%), United States (15.32%), Canada (2.96%), and other countries (2.12%).[31]

The camu-camu tree is an important component of riparian vegetation in Peru and Brazil, and is especially abundant in Peruvian black water systems, i.e., those rivers that have deep, slow-moving channels that flow through forested wetlands and swamps.[5] Although wild populations of the tree are highly productive, with some studies estimating fruit production at 9,000 to 12,000 kg per hectare in wild populations, interest in maximizing economic returns has led to cultivation of the tree as a way to increase rural incomes and raise standards of living. In 1996, the Peruvian government promoted and funded "reforestation" projects of camu-camu on the floodplains of the Peruvian Amazon as a flood-resistant and potentially highly productive tree crop. By 2006, only 10% of fields planted for these projects were planted on sites on which mature forests had been removed, but it is possible that more extensive clearing of mature forests could occur as camu-camu becomes more widely cultivated.[5] This planting program has had mixed success. There has been a lack of technical support on how to care for the plant and many have not survived. Also, some of these new orchard systems are on higher ground and no longer as flooded, leading to an increase in pest problems (M. Martin, personal communication March 20, 2012). In Peru, about 10,000 families are involved in camu-camu cultivation with Ucayali State as the focal production area and secondarily Loreto State, a conservation area due to the presence of natural tree stands and small-scale plantations. Started in 1997, the Agro-exportation Program project for camu-camu cultivation was projected to include 5,000 hectares of camu-camu by 2010, with 2,500 distributed in the Ucayali region and 2,500 in Loreto, including natural groves.[32]

One study comparing the differences between the wild and cultivated trees found variability in morphology and phenology.[5] The wild trees usually fruit once per year, but cultivated camu-camu appears to be less seasonal, and flowers and fruits at all stages of development can be found on a single tree, with trees frequently experiencing 2 fruiting cycles within a 6-month period. However, farmers cultivating the trees were concerned that the yields from the planted stock were not as high as from wild trees. Based on the variations in phenology (season and climactic effects on plants) and morphology of cultivated trees, there is also concern that the vitamin C content from the fruit of these trees may not be as substantial as from those in the wild, although there are no published reports of analysis of vitamin C levels to substantiate this concern.[5]

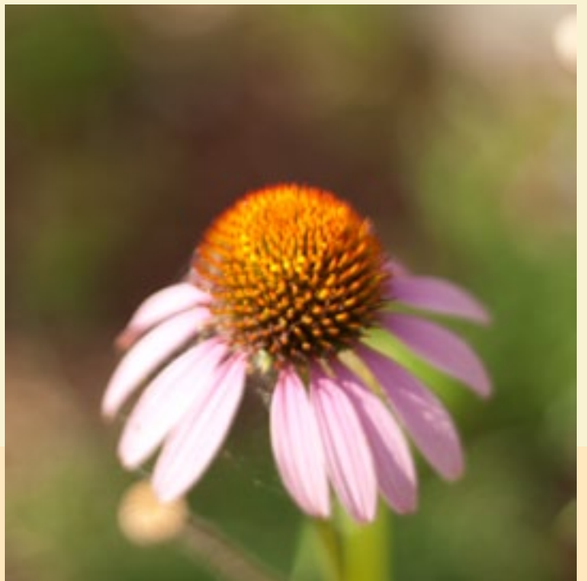
Now that widespread commercialization is taking place, a better understanding of the genetic variation is necessary to improve the productivity and vitamin C content of the cultivated tree. In addition, national and international market development will help local populations capitalize on farming of the fruit and its products.[10] In addition to more work on the cultivation of the fruit, there continues to be high potential for sustainable management of the wild stands. These wild areas still have huge amounts of production, and in fact are showing even higher densities of camu-camu plants per area. Thus, the fruit as an important NTFP should not be overlooked. In fact, much of the fruit continues to come from wild stands, although a shift to the more reliable cultivated plants is beginning to emerge (M. Martin, personal communication March 20, 2012). HG

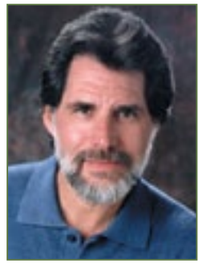
—Gayle Engels and Josef Brinckmann

REFERENCES

1. Taylor L. *The Healing Power of Rainforest Herbs*. Garden City Park, NY: Square One Publishers, Inc; 2005 Available at: http://www.rain-tree.com/camu.htm. Accessed February 27, 2012.
2. Castner J, Timme S, Duke J. *A Field Guide to Medicinal and Useful Plants of the Upper Amazon*. Gainesville, FL: Feline Press; 1998.
3. Peters CM, Balick MJ, Kahn F, Anderson AB. Oligarchic forest of economic plants in Amazonia: utilization and conservation of an important tropical resource. *Conservation Biology.* December 1989;3(4):341-349.
4. Rojas S, Yuyama K, Clement C, Ossamu-Nagao E. Diversidade genética em accesos do banco de germoplasma de camu-camu (*Myrciaria dubia* [H.B.K.] McVaugh) do INPA usando marcadores microssatélites (EST-SSR). *Revista Corpoica - Ciencia y Tecnología Agropecuaria.* 2011;12(1):51-64. Available at: www.corpoica.org.co/sitioweb/Archivos/Revista/6_Diversidade.pdf. Accessed March 25, 2012.
5. Penn JW. The cultivation of camu-camu (*Myrciaria dubia*): a tree planting programme in the Peruvian Amazon. *Forests, Trees, and Livelihoods.* 2006;16:85-101.
6. Instituto de Investigaciones de la Amazonía Peruana (IIAP). Evaluación y Selección de Colecciones Básicas del Germoplasma de Camu-camu. Iquitos, Perú: IIAP. 2010. Available at: www.iiap.org.pe/cdpublicaciones2011/documentos/pdf/PROBOSQUES/PU/35.pdf. Accessed March 25, 2012.
7. Dostert N, Roque J, Brokamp G, Cano A, La Torre MI, Weigend M. Factsheet: Datos botánicos de Camu Camu. Berlin, Germany: Botconsult. May 2009. Available at: www.botconsult.de/downloads/Camu_Camu_factsheet_final.pdf. Accessed March 25, 2012.
8. Duke JA, Bogenschutz-Godwin MJ, Ottesen AR. *Duke's Handbook of Medicinal Plants of Latin America*. Boca Raton, FL: CRC Press; 2009.
9. Justi KC, Visentainer JV, Evelázio de Souza N, Matsushita M. Nutritional composition and vitamin C stability in stored camu-camu (*Myrciaria dubia*) pulp. *Arch Latinoam Nutr*. 2000;50(4):405-408.
10. Potassium Supplement (Oral Route, Parenteral Route). Mayo

Clinic website. www.mayoclinic.com/health/drug-information/DR602373. Updated November 1, 2009. Accessed February 27, 2012.
11. Duke JA. *Myrciaria dubia.* Dr. Duke's Phytochemical and Ethnobotanical Databases. Available at: www.ars-grin.gov/duke/. Accessed February 27, 2012.
12. Inoue T, Komoda H, Uchida T, Node K. Tropical fruit camu-camu (*Myrciaria dubia*) has anti-oxidative and anti-inflammatory properties. *Journal of Cardiology*. 2008;52(2):127-132.
13. Codex Committee on Pesticide Residues. Draft revision of the Codex classification of foods and animal feeds at step 7: Fruit commodity groups. Rome, Italy: Codex Alimentarius Commission. February 2012. Available at: ftp://ftp.fao.org/codex/meetings/ccpr/ccpr44/pr44_09e.pdf. Accessed March 25, 2012.
14. European Commission Director General Health and Consumers. Myrciaria dubia. In: Novel Food Catalogue. Brussels, Belgium: European Commission. Available at: http://ec.europa.eu/food/food/biotechnology/novelfood/novel_food_catalogue_en.htm. Accessed March 25, 2012.
15. Hermann M. The impact of the European Novel Food Regulation on trade and food innovation based on traditional plant foods from developing countries. *Food Policy*. 2009;34:499-507. Available at: www.biomega.eu/deutschland/plaintext/downloads/090815-the-impact-of-the-european-novel-food-r.pdf. Accessed March 25, 2012.
16. European Food Safety Authority (EFSA) Panel on Dietetic Products, Nutrition and Allergies (NDA). Scientific Opinion on the substantiation of health claims related to vitamin C and protection of DNA. *EFSA Journal*. 2009;7(9):1226. Available at: www.efsa.europa.eu/en/scdocs/doc/1226.pdf. Accessed March 25, 2012.
17. World Trade Organization Committee on Sanitary and Phytosanitary Measures. Communication from Peru: Regulation 258/97 of the European Parliament and of the Council Concerning Novel Foods. Geneva, Switzerland: World Trade Organization. June 7, 2011.
18. European Commission Health & Consumers Directorate. Cosmetic Ingredients and Substances (CosIng®) Database. Brussels, Belgium: European Commission. Available at: http://ec.europa.eu/consumers/cosmetics/cosing. Accessed March 24, 2012.
19. Muller V. Whole World Botanicals Inc. FDA Notification Letter for Royal Camu. College Park, MD: Food and Drug Administration. July 9, 2004. Available at: www.fda.gov/ohrms/dockets/dailys/04/aug04/081704/97s-0162-let14406-vol125.pdf. Accessed March 25, 2012.
20. Health Canada. Natural Product Number (NPN) 00361828. In: Licensed Natural Health Products Database. October 16, 2007. Available at: http://webprod3.hc-sc.gc.ca/lnhpd-bdpsnh/index-eng.jsp. Accessed March 25, 2012.
21. Health Canada. Natural Product Number (NPN) 80026921. In: Licensed Natural Health Products Database. Available at: http://webprod3.hc-sc.gc.ca/lnhpd-bdpsnh/index-eng.jsp. Accessed March 25, 2012.
22. Health Canada. Myrciaria dubia fruit flavour. In: Natural Health Products Ingredients Database. Available at: http://webprod.hc-sc.gc.ca/nhpid-bdipsn/search-rechercheReq.do. Accessed March 25, 2012.
23. Instituto Peruano de Productos Naturales. Comisiones: Comites y grupos de trabajos donde el IPPN participa. Lima, Peru: IPPN: Available at: www.ippn.org.pe/index.php?option=com_content&view=article&id=52&Itemid=30. Accessed March 24, 2012.
24. Instituto Nacional de Pesquisas da Amazônia (INPA). Relatório Annual: Anexos. Manaus, Brazil: INPA. 2011. Available at: www.inpa.gov.br/internas/diretoria/relatorios/TCG/INPA_TCG_2011_Anexo.pdf. Accessed March 24, 2012.
25. Yuyama LKO, Rosa RD, Aguiar JPL, Nagahama D, Alencar FH, Yuyama K, Cordeiro WO, Marques HO. Açaí (*Euterpe oleracea* Mart.) e Camu-Camu (*Myrciaria dubia* (H.B.K.) Mc Vaugh) possuem ação anti anêmica? *Acta Amazônica*. 2002;32(4): 625-633. Available at: http://acta.inpa.gov.br/fasciculos/32-4/PDF/v32n4a08.pdf. Accessed March 24, 2012.
26. De Souza Schmidt Gonçalves AE, Lajolo FM, Genovese MI. Chemical composition and antioxidant/antidiabetic potential of Brazilian native fruits and commercial frozen pulps. *J Agric Food Chem*. 2010;58:4666-4674.
27. Chirinos R, Glarza J, Betalleluz-Pallardel I, Pedreschi, R, Campos D. Antioxidant compounds and antioxidant capacity of Peruvian camu camu (*Myrciaria dubia* (H.B.K.) McVaugh) fruit at different maturity stages. *Food Chemistry*. 2010;120:1019-1024.
28. Zanatta CF, Cuevas E, Bobbio FO, Winterhalter P, Mercadante AZ. Determination of anthocyanins from camu-camu (*Myrciaria dubia*) by HPLC-PDA, HPLC-MS, and NMR. *J Agric Food Chem.* 2005;53:9531-9535.
29. Franco MRB, Shibamoto T. Volatile composition for some Brazilian fruits: umbu-caja (*Spondias cytherea*), camu-camu (*Myrciaria dubia*), araça-boi (*Eugenia stipitata*), and cupuaçu (*Theobroma grandiflorum*). *J. Agric. Food Chem.* 2000;48:1263-1265.
30. Sistema Integrado de Información de Comercio Exterior (SIICEX). Exportaciones del producto camu camu según sus principales presentaciones en US$ 1998 – 2012. Lima, Peru: SIICEX. Available at: www.siicex.gob.pe/siicex/apb/ReporteProducto.aspx?psector=1025&preporte=prodpres&pvalor=1920. Accessed March 25, 2012.
31. Sistema Integrado de Información de Comercio Exterior (SIICEX). Ficha técnica Camu camu. Lima, Peru: SIICEX. November 2009. Available at: www.siicex.gob.pe/siicex/resources/fichaproducto/611423054rad1DE75.pdf. Accessed March 25, 2012.
32. Oliva-Cruz CA. Camu camu *Myrciaria dubia* (H.B.K.) Mc Vaugh, a socio-economically important native species in the Peruvian Amazon. *Amazon Agroforestry*. December 2009;1(2):16-17. Available at: www.worldagroforestry.org/downloads/publications/PDFs/NL09158.PDF. Accessed March 25, 2012.





dear *reader*

Adulteration of "Grapefruit Seed Extract," etc.

As a part of our ongoing series dealing with accidental and intentional adulteration of botanical raw materials sold for a variety of uses (*e.g.*, food flavors, dietary supplements, cosmetics, non-prescription medicines, *et al.*), we present John Cardellina's review of 10 analytical papers published since 1991 on an ingredient called "grapefruit seed extract," for which the results show that many or possibly most of these materials appear to have been adulterated with synthetic industrial disinfectants like triclosan, benzalkonium chloride, and/or benzethonium chloride. According to all of the available papers reviewed in this article, one or more of these synthetic compounds appear in most of the analyzed samples; however, none of these synthetic disinfectant compounds were found in extracts made in the research laboratories from actual grapefruit seeds (*Citrus* x *paradisi*), and all of the "grapefruit seed extracts" that did not contain the synthetics exhibited no experimental antimicrobial activity. This evidence is strongly suggestive of intentional adulteration. This situation is especially curious, given the fact that there does not appear to be any historical or traditional medicinal use of grapefruit seed, or preparations made from it in any treatises or monographs in traditional literature, pharmacopoeial compendia, etc.

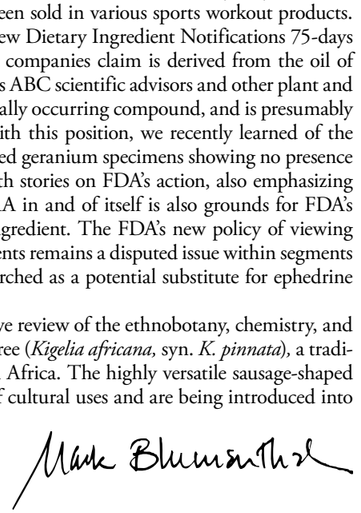
Information on the Internet, some of it associated with companies that market GFSE, claims that these compounds are produced by a proprietary chemical process from the naturally occurring chemicals in grapefruit seeds. Dr. Cardellina and other chemical experts with whom we have consulted believe that such chemical synthesis does not conform with any known chemistry or chemical pathways.

It is unclear to what extent any products currently sold in the market in the US and elsewhere reflect the chemical profiles found in any of these analyses, or to what extent, if any, there may be safety concerns. To date, there does not appear to be. Nevertheless, in our view, this is a matter of possible misbranding or adulteration or both that should be immediately researched by the Food and Drug Administration (FDA), and, if FDA analyses confirm those that are summarized in this article, regulatory action should be taken.

Some of the publications reviewed in Dr. Cardellina's article use the acronym "GSE" to refer to grapefruit seed extract. This same acronym has also been used to describe grape seed extract—an entirely different material from an entirely different plant—*i.e.*, *grapes* (*Vitis vinifera*) instead of *grapefruits*. Accordingly, we have created a new acronym, GFSE, instead of using GSE, to refer to the so-called grapefruit seed extract and we invite our colleagues in academia, the health professions, industry, and elsewhere to do the same in future publications and communications.

And, speaking of adulteration, as we were going to press, following months of controversy in the dietary supplement industry in the US and elsewhere, FDA issued Warning Letters to 10 companies that produce and/or market the controversial compound called DMAA (1,3 dimethylamylamine; or MHA, methylhexaneamine), an ingredient that has been sold in various sports workout products. According to FDA, the companies failed to provide New Dietary Ingredient Notifications 75-days prior to marketing the ingredient, which some of the companies claim is derived from the oil of geranium *(Pelargonium graveolens)*. However, numerous ABC scientific advisors and other plant and chemical experts have stated that DMAA is *not* a naturally occurring compound, and is presumably synthetically chemically produced. And, consistent with this position, we recently learned of the forthcoming publication of geranium oil from vouchered geranium specimens showing no presence of DMAA. Industry-oriented e-newsletters are rife with stories on FDA's action, also emphasizing FDA's position that the synthetic nature of the DMAA in and of itself is also grounds for FDA's wanting to remove it from the market as a dietary ingredient. The FDA's new policy of viewing synthetic botanical constituents as non-dietary ingredients remains a disputed issue within segments of the dietary supplement industry. DMAA was researched as a potential substitute for ephedrine in the late 1940s.

Our cover story this issue is Simon Jackson's extensive review of the ethnobotany, chemistry, and pharmacology of various plant parts from the sausage tree (*Kigelia africana,* syn. *K. pinnata*), a traditional herbal remedy from many areas of sub-Saharan Africa. The highly versatile sausage-shaped fruits and other parts of this tree cover a wide range of cultural uses and are being introduced into the US and elsewhere.



ABC Advisory Board

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

HERBALGRAM

The Journal of the American Botanical Council

Number 94 • May - July 2012

features

Sausage Tree *Kigelia pinnata.*
Photo ©2012 PhytoTrade Africa

departments

On the Cover
Sausage Tree *Kigelia pinnata*
Photo ©2012 PhytoTrade Africa

Published by the American Botanical Council, P.O. Box 144345, Austin, TX 78714-4345.

Subscriptions to *HerbalGram* are a benefit of ABC membership at every level. One year memberships: Individual $50; Academic $100; Professional $150; Organization $250; Retailer $250; HerbClip Service $600; Corporate; Sponsor. Add $20 for memberships outside of the U.S. Student and Senior discounts are available. For information about Corporate or Sponsor Memberships, contact Denise Meikel at denise@herbalgram.org or 512-926-4900.

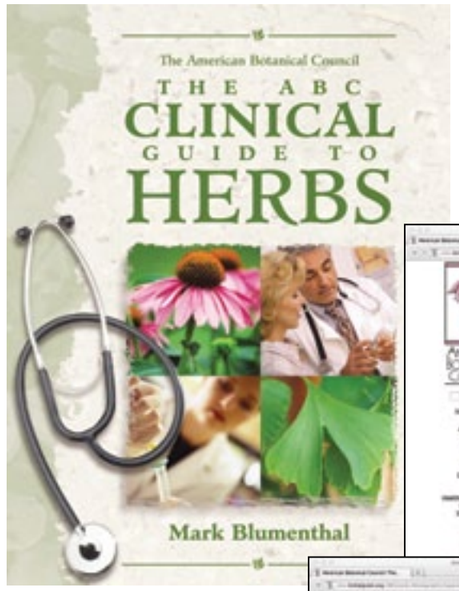
HerbalGram® is printed on recycled paper at Craftsman Printers, Inc. Lubbock, Texas

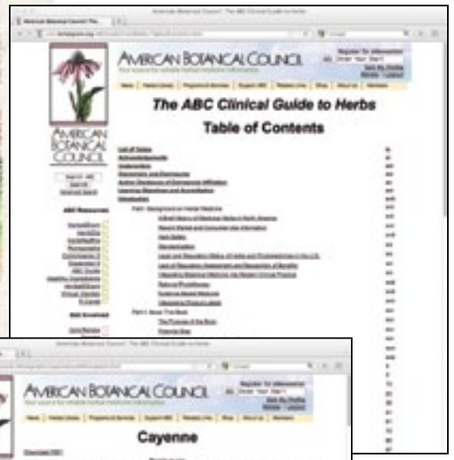
The ABC Clinical Guide to Herbs Now Available Online

Electronic Publication Enriches Comprehensive Herbal Reference Book

The American Botanical Council (ABC) recently announced online publication of *The ABC Clinical Guide to Herbs* at www.herbalgram.org. Originally released as a reference book in 2003, *The Guide* is a 400-plus page, science-based, peer-reviewed text containing complete therapeutic monographs and clinical study details on 30 of the best-selling herbs in the United States at that time. Most of these herbs are still present on the lists of top-selling herbs used as teas or dietary supplements.

Adding the Guide to ABC's online resources always has been part of the organization's web content plan, as was the case with the online versions of ABC's first 2 books: *The Complete German Commission E Monographs–Therapeutic Guide to Herbal Medicines* (1998) and *Herbal Medicine: Expanded Commission E Monographs* (2000). Online publication of *The Guide* helps carry out ABC's nonprofit educational mission to make as much credible information on herbs and phytomedicines available to the widest audience as possible.





ABC members who use the online Guide will benefit from the electronic version's global and advanced search functions and enhanced interactivity, which enables users to view any specific section of the Guide by simply clicking their selection from the hyperlinked Table of Contents. The user can also download PDFs of the full monographs—including the main monograph, the clinical overview, and the patient information sheet for each herb—as well as PDFs of the proprietary product monographs.

Because the book was published in 2003, ABC has taken the opportunity to correct any typographical errors, and also has updated and revised several sections. The "Accreditation for Continuing Education" page, for example, has been updated and the expired test and applications for continuing education credit are no longer available. Several parts of the online version also link to more recent information. The outdated "Introduction on Recent Market and Consumer Use Information" and "Top-Selling Herbal Supplements in Food, Drug, and Mass Market Retail Outlets" sections now link to the Market Report section of ABC's printed, peer-reviewed journal, *HerbalGram,* so that the user will always have access to the most recent data.

Additionally, ABC has clarified that the Recent Studies were recent "as of April 2003" and provide links to *HerbalGram* and HerbClips online for information on new research developments and relevant breaking news. Additionally, the online Guide now states that Company Contact information in the Branded Products sections of the monographs and in the Appendix was current "as of April 2003" and has not been updated due to the ease of using Internet search engines to find up-to-date and revised contact information for clinically tested branded product manufacturers.

A benefit of ABC membership at the Professional level and above, the online Clinical Guide can be accessed on ABC's homepage by clicking the "ABC Guide" link, located on the left side of the page, or the "Programs & Services" link, at the top of the homepage. For a limited time, ABC is offering members at the Individual and Academic levels the opportunity to upgrade to the Professional level at a 20% discounted rate. For more information, contact ABC's membership department. HG

—Gayle Engels and Lindsay Stafford

American Botanical Council Welcomes 15 New Advisory Board Members

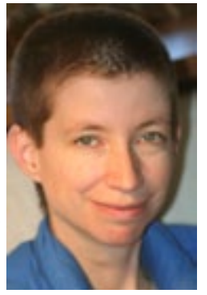
New Advisors Represent a Wide Range of Expertise in Herbal Matters

The American Botanical Council (ABC) announced in early February the addition of 15 new members to its Advisory Board. These esteemed individuals—with diverse academic backgrounds ranging from nutrition, neurology, and naturopathy to anthropology, botany, and biochemistry—are committed to promoting healthier living through herbal and plant-based medicine. Advisory Board members volunteer their time to peer review articles, papers, and other documents that appear in *HerbalGram*, HerbalEGram, HerbClips, and various ABC publications. Additionally, *HerbalGram* editors seek feedback and advice from Advisory Board members on issues such as research questions, article ideas, ABC policies, book reviews, and much more.

The new Advisory Board members include a botanist, an ethnobotanist, 4 pharmacognosists and medicinal plant researchers, 2 natural product chemists, a neurologist, 2 naturopathic physicians, 2 herbalists, a nutritional biochemist, and an oncology researcher.

"We are deeply grateful to include these experts on the ABC Advisory Board," said ABC Founder and Executive Director Mark Blumenthal. "In many cases, adding these people to our Advisory Board simply formalizes an already established, long-term relationship in which many of these friends and colleagues have been contributing their time and expertise to ABC and many of its publications as expert peer reviewers."

Following are the names and brief bio-sketches of the new ABC Advisory Board members.



Wendy Applequist, PhD, is a botanist and an associate curator at the Missouri Botanical Garden's William L. Brown Center, an institution dedicated to preserving traditional knowledge of useful plants. At the Center, Dr. Applequist manages natural products discovery programs and research efforts involving medicinal plants. She currently serves as an associate editor of *Economic Botany* and the secretary of the international Nomenclature Committee for Vascular Plants. Her first book, *The Identification of Medicinal Plants: A Handbook of the Morphology of Botanicals in Commerce,* was published in 2006 by the Missouri Botanical Garden and ABC.

K. Hüsnü Can Başer, PhD, served as the dean of the Faculty of Pharmacy and the director of the Medicinal and Aromatic Plant and Drug Research Centre (TBAM) at Anadolu University in Turkey. He is currently a member of the World Health Organization's Expert Advisory Panel on Traditional Medicine and the Turkish Pharmacopoeia Commission. His research interests include essential oils, alkaloids, and natural products. In recent years, 2 plant species have been named in his honor: *Origanum husnucan-basari* (Lamiaceae) and *Aristolochia baseri* (Aristolochiaceae). He is the co-editor of the *Handbook of Essential Oils: Science, Technology, and Applications*, published by CRC Press in 2009.

Rudolf Bauer, PhD, is considered one of the world's foremost experts on echinacea (*Echinacea* spp., Asteraceae). Currently, he is a professor in the Department of Pharmacognosy and head of the Institute of Pharmaceutical Sciences at the University of Graz in Austria. Bauer received his PhD under the supervision of Prof. Hildebert Wagner, PhD—one of the leading experts on adaptogenic medicinal plants—at the University of Munich in Germany. From 2002 to 2007 he served as the president of the International Society for Medicinal Plant Research. He is also the co-editor of *Planta Medica* and leads the Traditional Chinese Medicine Research Center at Graz. His research interests include quality control and standardization of herbal medicine and structural research of biologically active plant constituents. Bauer was awarded ABC's Norman R. Farnsworth Excellence in Botanical Research Award in 2010.

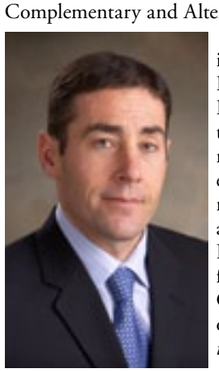
Chun-Tao Che, PhD, is the recently appointed Norman R. Farnsworth Professor of Pharmacognosy in the College of Pharmacy at the University of Illinois at Chicago, where he received his PhD in 1982. Prof. Che is the associate editor of *Pharmaceutical Biology* and an editorial board member of the *Journal of Ethnopharmacology.* His research interests include pharmaceutical applications of herbal preparations, quality control standardization, and the development of evidence-based herbal medicine to support traditional medicine use in modern society. He has been cited in more than 240 scientific papers.

Bevin Clare, RH, CNS, is a licensed nutritionist and registered clinical herbalist based in Laurel, Maryland. She is the chair of the Masters of Science Herbal Medicine Program at the Tai Sophia Institute, an adjunct assistant professor at the Massachusetts College of Pharmacy, and an asso-

ciate professor at the New York Chiropractic College. Clare is the current vice-president of the American Herbalists Guild, a member of the board of directors for United Plant Savers, and an advisory board member of the International Research Group for the Conservation of Medicinal Plants.

Tori Hudson, ND, has been in practice as a naturopathic physician for 28 years, and is a clinical professor at 3 institutions—the National College of Natural Medicine, the Southwest College of Naturopathic Medicine, and Bastyr University. Specializing in natural therapies for women's health, she serves as the program director of the Institute of Women's Health and Integrative Medicine and as the medical director and co-founder of "A Woman's Time" clinic, both in Portland, Oregon. Dr. Hudson is the author of the *Women's Encyclopedia of Natural Medicine*, she was chosen as the 1999 Naturopathic Physician of the Year by the American Association of Naturopathic Physicians and she was the 2009 recipient of the Natural Products Association's Pioneer Award. She is also the director of research, development, and education for Vitanica, a dietary supplement company for women's health.

David Kroll, PhD, is director of Science Communications and investigator in the Laboratory of Microbiology and Genomics at the new Nature Research Center of the North Carolina Museum of Natural Sciences in Raleigh. Dr. Kroll is also Professor of Science Communications in the masters of science program in technical communications at North Carolina State University. Previously, he worked as a senior research pharmacologist at the Research Triangle Institute and was assistant and associate professor of Pharmacology and Toxicology at the University of Colorado School of Pharmacy. Dr. Kroll's current research involves finding anti-cancer and chemoprotective compounds from milk thistle (*Silybum marianum,* Asteraceae). He recently completed a term on the editorial board of the Physician's Data Query at the National Cancer Institute's (NCI) Office of Cancer Complementary and Alternative Medicine and serves routinely as a reviewer for NCI and the National Center for Complementary and Alternative Medicine.



Douglas "Duffy" MacKay, ND, is the vice-president of Science and Regulatory Affairs at the Council for Responsible Nutrition, a trade association representing dietary supplement manufacturers and ingredient suppliers. Dr. MacKay is a licensed naturopathic doctor and works part-time at the Integrative Medical Center in Kensington, Maryland. He is a delegate for the United States Pharmacopeial Convention and currently serves on editorial boards of the *Alternative Medicine Review* and the *Natural Medicine Journal*. He previously worked in the natural products industry at Nordic Naturals and Thorne Research.

Mark Messina, PhD, is the president of Nutrition Matters, Inc., a nutrition consulting firm, and the executive director of the Soy Nutrition Institute. He also works as an adjunct associate professor in the Department of Nutrition at Loma Linda University. His research interests include the health effects of soy foods (*Glycine max*, Fabaceae) and soybean isoflavones. On these topics, Dr. Messina has given more than 500 presentations and published more than 60 articles. He was the 2011 recipient of the United Soybean Board's Outstanding Achievement Award.

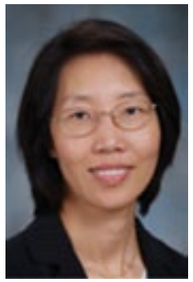
Susan Murch, PhD, a natural products chemist, is an associate professor and Canada Research Chair in Natural Products Chemistry at the University of British Columbia. She also serves as a research associate for the National Tropical Botanical Garden in Hawaii, where she conducts research on tropical plant conservation and development. Dr. Murch served as the president of the Natural Health Products Research Society of Canada from 2010-2011 and is a member or fellow of more than 10 scientific societies. Her research interests include plant metabolomics, plant neurochemicals, and the conservation of breadfruit (*Artocarpus altilis,* Moraceae). She is the co-author of a recent feature article on osha root (*Ligusticum porteri,* Apiaceae) in a 2011 issue of ABC's peer-reviewed journal *HerbalGram*.

Nicholas Oberlies, PhD, a pharmacognosist and natural products chemist, is an associate professor in the Department of Chemistry and Biochemistry at the University of North Carolina at Greensboro. Previously, he worked in the Natural Products Laboratory at the Research Triangle Institute in North Carolina. Dr. Oberlies is on the editorial board of *Progress in the Chemistry of Organic Natural Compounds*. He serves the natural products community as an engaged scientist and regular contributor and reviewer of the literature.

John Rashford, PhD, is a professor of anthropology at the College of Charleston, where he teaches courses such as "Ethnoscience and Ethnobiological Classification," "Ecological Anthropology," and "Gardens in Charleston: An Ethnobotanical View." His research interests include baobab trees (*Adansonia gregorii,* Malvaceae), ethnobotany, economic anthropology, and ecology. Dr. Rashford is currently president of the Board of the Charleston Museum as well as a board member of the National Tropical Gardens and the Gaylord and Dorothy Donnelley Foundation.

Ethan Russo, MD, is a board-certified neurologist, a psychopharmacology researcher, and the senior medical advisor to GW Pharmaceuticals, the UK manufacturer of a patented, multi-standardized, clinically tested extract of *Cannabis sativa* (Cannabaceae). Dr. Russo previously served as an affiliate associate professor in the Department of Pharmacology at the University of Washington School of Medicine and a visiting professor at the Institute of Botany for the Chinese Academy of Sciences. He is the author of the *Handbook of Psychotropic Herbs* (Haworth Press, 2001) and was previously the secretary of the International Cannabinoid Research Society and the chairman for the International Association for Cannabinoid Medicines.

Richard "Ric" Scalzo is the president, CEO, and founder of Gaia Herbs, Inc., a grower and manufacturer of herbal wellness solutions. His interests include herbal medicine research, herbal formulation processes, and ecological sustainability. Scalzo serves on the board of the Research Center for Natural and Social Resources (CIRENAS) and is the author of *Herbal Solutions for Healthy Living* (Herbal Research Publications, 2001). He was awarded an honorary doctorate in Naturopathic Sciences from the Southwest College of Naturopathic Medicine.



Peiying Yang, PhD, is an assistant professor in the Department of General Oncology in the Section of Integrative Medicine at the University of Texas, M.D. Anderson Cancer Center (MDACC). She received her BS and MS from the Beijing University of Traditional Chinese Medicine and her PhD in Nutritional Science from the University of Maine, Orono, in 1997. Dr. Yang has been actively involved in the International Oncology Center—a collaboration between MDACC and Fudan University Cancer Hospital in Shanghai, China—where she examines the role of Chinese Medicine in cancer treatment and prevention. She is a member of the Society for Integrative Oncology, the American Association for Cancer Research, and the American Society of Mass Spectrometry. HG

ABC Presents 2012 Botanical Excellence Awards

The American Botanical Council held the 7th Annual ABC Botanical Celebration and Awards Ceremony on March 8, 2012 in Anaheim, CA. As in previous years, ABC's event was held in conjunction with the Natural Products Expo West trade show and Nutracon scientific conference.

7TH ANNUAL AMERICAN BOTANICAL Celebration

The event, held at the Marriott Anaheim, was attended by approximately 300 ABC Sponsor Members, Corporate Members, and other supporters of ABC's nonprofit educational mission. The evening was filled with enthusiastic conversations, opportunities to renew old relationships and forge new ones, delicious food and drink and, of course, some of the honored award recipients.

The awards program itself began with a slide show of entertaining cartoons which got the crowd laughing and included gracious comments from Loren Israelsen of United Natural Products Alliance recognizing the unique role ABC plays in the natural products community. ABC Board of Trustees Chairman Steven Foster announced the ABC James A. Duke Excellence in Botanical Literature Award recipients, including, for the first time, 2 categories—Consumer/Popular category awarded to Bharat Aggarwal, PhD, and the Reference/Technical Category awarded to Roy Upton.

ABC Founder and Executive Director Mark Blumenthal presented Bioforce AG with the ABC Varro E. Tyler Commercial Investment in Phytomedicinal Research Award, which was accepted by Pierce Sioussat of Bioforce USA. Previous ABC Farnsworth Award recipient Joseph M. Betz, PhD, presented the ABC Norman R. Farnsworth Excellence in Botanical Research Award to Djaja Doel Soejarto, PhD. This was a particularly poignant award as Professor Soejarto is the last recipient of this award personally selected by the late Prof. Norman Farnsworth.

ABC's James A. Duke Excellence in Botanical Literature Awards

Herbal Microscopy Book Receives Award for Reference and Technical Book Category

ABC presented the American Herbal Pharmacopoeia's *Botanical Pharmacognosy: Microscopic Characterization of Botanical Medicines* with this year's ABC James A. Duke Excellence in Botanical Literature Award in the reference and technical book category. The book was published by CRC Press in 2011.

The award, created in 2006 in honor of noted economic botanist and author James A. Duke, PhD, is given annually to a book that provides a significant contribution to literature in the fields of botany, taxonomy, ethnobotany, phytomedicine, or other disciplines related to the vast field of medicinal plants. Among his long and prestigious career achievements in economic botany and ethnobotany at the United States Department of Agriculture, Dr. 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 is Director Emeritus.

The AHP Microscopy book was edited by senior editor Roy Upton, executive director of AHP. Other editors include Alison Graff, PhD, a rare plant conservationist for the state of California; the late Georgina Jolliffe, PhD, formerly a senior lecturer in pharmacognosy at Chelsea College (now King's College) in the United Kingdom; Reinhard Länger, PhD, an herbal medicinal products expert at the Austrian Medicines Agency; and Elizabeth Williamson, PhD, a professor of pharmacy and director of practice of the School of Pharmacy at the University of Reading in the United Kingdom.[1]

Loren Israelsen of United Natural Products Alliance

AHP's 773-page *Botanical Pharmacognosy: Microscopic Characterization of Botanical Medicines* is organized into 2 sections: a 10-chapter introduction to the art of microscopy and a botanical microscopy atlas. The atlas, which comprises roughly three-quarters of the book, contains more than 135 detailed descriptions of the histology (cell structure) of some of the most commonly used medicinal plants in North America and around the world.[1]

"In developing the AHP monographs, we realized that botanical microscopy was *the* primary form of crude plant part identification used for [more than] 100 years," said Upton (email, February 14, 2012). "This gave us the idea that it would be good to have a textbook, as some of the plants sold in the marketplace today as dietary supplements and teas had never been microscopically analyzed or recorded."

In his preface to the book, Upton describes the unique importance that microscopy has within pharmacognosy (the study of medicines of natural origin) and its status as a "dying art" in North America and Europe.[1] "Our work in developing microscopic characterizations for AHP monographs as a fundamental identity test has underscored for us the value and importance of microscopy as a quality assessment tool," he said. "We embarked upon this project as our way of helping to preserve and reenergize this scientific discipline."

While previous microscopy texts presented limited tools for plant identification—often relying on single, unconfirmed botanical specimens with pictures of only the powdered substance—AHP's text contains meticulously authenticated samples with full-color images of plant parts and powders as well as intricate line drawings. Upton said he hopes the textbook will help readers "recognize the utility of microscopy as a low cost, low environmental impact, and effective quality assessment tool for both identification of plants [and] species and for the detection of impurities [*e.g.*, adulterants]."

The late Professor Norman R. Farnsworth, PhD, in his foreword to the book, praised Upton's work, which was 10 years in the making.[1] "I have always found that Roy Upton, the major driver for this work, has a long history of producing botanical monographs and his work and passion for botanicals has been clear, thorough, and accurate, which is exemplified in this textbook of botanical microscopy," wrote Professor Farnsworth. "It will soon become the major authority on the microscopic identification of crude botanical ingredients." Prof. Farnsworth was one of the world's most well-known and respected medicinal-plant researchers. In addition to his many academic, organizational, and advisory positions, he was a co-founder of ABC.

"With the increasing need for accurate, reliable, authoritative information on ensuring proper plant identification as part of the Good Manufacturing Practices requirements for the herb and dietary supplement industry, AHP's microscopy reference book is a monumental contribution to the herb industry, to the natural products and natural medicine research and healthcare communities who research and/or recommend these products, and, eventually, to consumers who use herbal products for their health," said Blumenthal.

Noted author and photographer Steven Foster, chairman of the Board of Trustees of ABC, said, "Roy Upton's excellent reference manual will become a key part of the herb quality control formula for members of industry, researchers, and regulators for decades to come."

Upton, a practicing herbalist since 1981, is the founder, executive director, and editor of the American Herbal Pharmacopoeia. He is also a co-founder, past president, and vice-president of the American Herbalists Guild and serves on the Committee of Revision for the United States Pharmacopeia.

The *American Herbal Pharmacopoeia: Botanical Pharmacognosy–Microscopic Characterization of Botanical Medicines* retails for $169.95 and can be purchased from ABC's eStore.

Healing Spices Book Receives Award for Consumer and Popular Books Category

ABC gave its Duke Award in the newly designated consumer and popular books category to *Healing Spices: How to Use 50 Everyday and Exotic Spices to Boost Health and Beat Disease*, written by Bharat B. Aggarwal, PhD, and published by Sterling Publishing in 2011.

Dr. Aggarwal, author of *Healing Spices*, has been a faculty member at the University of Texas M.D. Anderson Cancer Center in Houston, Texas, since the late 1980s. Before joining M.D. Anderson, Dr.


Mark Blumenthal of ABC, Terry Lemerond of EuroPharma, Greg Ris of Indena USA

Aggarwal worked for Genentech Inc., where his work led to the discovery of TNF-alpha and TNF-beta, 2 essential components of the human immune system. This discovery has been heralded by many as a highly significant scientific breakthrough. Among numerous publications he is also the lead editor of *Inflammation, Lifestyle and Chronic Diseases: The Silent Link* (CRC Press, 2011) and *Molecular Targets and Therapeutic Uses of Spices: Modern Uses for Ancient Medicine* (World Scientific Publishing Co., 2009).

Dr. Aggarwal's current research involve cytokines—signaling molecules secreted by various cells in the human body—and the role of inflammation in cancer and other diseases, and how chemical components from various herbs, *e.g.*, turmeric (*Curcuma longa,* Zingiberaceae) can modulate these molecules.[2]

"Virtually all the chronic diseases are caused by disregulated inflammation," said Dr. Aggarwal (oral communication, February 20, 2012). "We need to find ways to control that inflammation. Spices are one of the best ways to do that. Vasco de Gama and Christopher Columbus, way back in the 15th century—even they knew spices were good for something. Here, 500 years later, we still have no doubt that they are good for something, but the question is how to use them in everyday life. That's where I thought I could help."

Dr. Aggarwal was approached by a publisher 2 years ago to create a book on the health benefits of various spices. At the time, he was assisting McCormick—the largest spice maker in the United States—with a website called Spices for Health.

Healing Spices covers 50 common spices and their beneficial qualities. The book provides detailed historical information, medicinal uses, and some recipes. It is organized as a user-friendly guide to the healing properties of spices and offers descriptions of specific ailments and conditions that can benefit from each spice.[3]

Dr. Duke, who keeps *Healing Spices* on his bookshelf of most-frequently used books, said that Dr. Aggarwal's book "is important to medical botany … [and] will appeal to most health-concerned readers" (e-mail, February 20, 2012).

Healing Spices has been received so well that its publisher has asked for a follow-up book. "Knowing about spices is one thing, but knowing how to use them is something else," said Dr. Aggarwal. "We are talking about a cookbook now; a healthy spice cookbook to teach people how to use spices."

Dr. Aggarwal, in addition to his research on spices, has identified more than 50 compounds from dietary sources and traditional medicinal herbs that interrupt cell-signaling inflammatory pathways; some of these have been subjected to animal testing and have started human clinical trials.[2] If he were to recommend 1 spice for daily use, he says he would recommend turmeric, which contains important anti-inflammatory compounds known as curcuminoids.

"Over the past 3 to 4 decades, millions of consumers in the United States and worldwide have become aware of the many health benefits of herbs and many common culinary spices," said ABC's Blumenthal. "Much of the recent research that supports some of this growing awareness has been conducted by Dr. Aggarwal and his many associates. ABC is pleased to be able to recognize his important contributions by granting him this award."

Healing Spices can be purchased for $24.95 from the ABC eStore.

Professor Doel Soejarto Receives ABC's Farnsworth Excellence in Botanical Research Award

As noted above, ABC gave this year's Norman R. Farnsworth Excellence in Botanical Research Award to Professor Djaja Doel Soejarto, PhD, of the University of Illinois – Chicago (UIC).

The award's namesake is ABC's co-founding Board of Trustees member, the late Prof. Norman R. Farnsworth, PhD. Dr. Farnsworth was a research professor of pharmacognosy and senior university scholar at the College of Pharmacy at UIC. The medicinal plant community lost a champion when he died last year at the age of 81. ABC will continue to present this award each year to a person or institution that has made significant contributions to botanical and/or pharmacognostic research (i.e., research on drugs of natural origin, usually from plants).


Prof. Doel Soejarto, PhD

Like the renowned individual for whom the award was named, Dr. Soejarto is a professor of pharmacognosy in the department of medicinal chemistry and pharmacognosy at the College of Pharmacy at UIC. He also teaches biology in UIC's department of biological sciences.

"My immediate reaction on receiving the notification about the ABC Norman Farnsworth Excellence in Botanical Research Award was a downcast feeling, 'Have I done something worthwhile for such an award?'," said Dr. Soejarto. "After a reflection, that feeling soon turned into elation, and thankfulness to the American Botanical Council. All my significant accomplishments during the past 30 years have been associated with Norman Farnsworth. Specifically, I have accomplished my professional successes because of the mentorship of this great Professor" (e-mail, February 24, 2012).

"The Farnsworth award's being granted to Prof. Soejarto is particularly poignant this year," said Blumenthal. "Prof. Farnsworth himself chose Prof. Soejarto a few months before he died last September. Thus Prof. Soejarto is the last person to receive this award with Prof. Farnsworth's 'blessing.'"

A native of Indonesia, Dr. Soejarto earned his master's and doctorate degrees at Harvard University, where his primary focuses were biology and botany. He has held various professorial positions at UIC since 1979. Some of the highlights of his scientific career include the completion of the taxonomic revision of the genus *Saurauia*, the discovery of anti-HIV calanolides from a pair of *Calophyllum* species, and the founding of the herbarium at the University of Anitoqiua in Colombia.

As the principal investigator of The Vietnam-Laos International Cooperative Biodiversity Group—"a program for collaborative research in the pharmaceutical studies" housed in UIC's College of Pharmacy—Dr. Soejarto leads the group in inventorying the medicinal plants of Vietnam's Cuc Phuong National Park, analyzing plants in Vietnam and Laos for drug development potential, supporting economic development in Vietnam and Laos, and making information on Cuc Phuong's plants available on the web.[4] Fifty-seven new and active compounds have been discovered thus far.

According to Dr. Soejarto, the concept of "multidisciplinary collaboration" in scientific research was one of the most significant things he learned from Dr. Farnsworth. It ultimately "lured him into the study of medicinal plants" and "enabled [him] to find a niche in the endeavor to discover new bioactive molecules from plants."

"Doel Soejarto has devoted almost a half century to the multidisciplinary study of medicinal plants, including taxonomy, ethnobotany, biodiversity inventory and conservation, drug discovery, and intellectual property rights of indigenous people," said Harry Fong, PhD, professor emeritus of pharmacognosy at UIC. "His pursuit in each of these areas of botanical research is laser-focused. It can be said that if all around him is in a state of chaos, Doel will not be deterred from his task at hand. His sense of duty, his devotion to the pursuit of knowledge generation, his desire and enthusiasm to advance botanical sciences for the good of humanity are the essence of his being" (e-mail, February 28, 2012).

This year, Dr. Soejarto also has been honored by the Society for Economic Botany as its Distinguished Economic Botanist. He sits on the editorial boards of *Pharmaceutical Biology, Tropical Ethnobiology,* and the *Journal of Ethnopharmacology*, the last of which he previously edited for 14 years. In addition, he is a member of a number of prestigious professional organizations, and his articles have been featured in *Phytochemistry*, *Pharmaceutical Biology*, and the *Journal of Genetics and Applications*.

Swiss Herbal Products Company Bioforce Noted for Scientific and Clinical Research

ABC bestowed its annual Varro E. Tyler Award for Commercial Investment in Phytomedicinal Research to Bioforce AG, a Swiss herbal products manufacturer that spends approximately $1 million on pharmacological and clinical research each year, according to company sources.[5]

"We were surprised and honored to receive this prestigious award and, at the same time, also proud to see that our efforts to invest in research are acknowledged," said Andreas Suter, head of medicine and product development at Bioforce AG (e-mail, November 28, 2012). "We share [Prof. Tyler's] views on phytotherapy, that the use [of] herbal medicine must not only be based on fascination but also on sound scientific data."

"Bioforce is a rare company in the global herbal community," said Blumenthal. "The company employs the highest quality levels of

Pierce Sioussat, left, Bioforce USA President, shown here with ABC's Mark Blumenthal, accepting the ABC Varro E. Tyler Commercial Investment in Phytomedicinal Research Award for Bioforce AG

sustainable farming practices while embracing the rich traditions of European herbal medicine, combining it with modern scientific research. These concepts—sustainability, tradition, and research—are at the core of the company's ethics and practices. Bioforce's continued investment in research is consistent with Prof. Varro Tyler's wish that all herb companies dedicate a portion of their revenues to researching the mechanisms and/or the efficacy of their botanical products."

The late Prof. Tyler—who has been described as one of the most respected men in late 20th century herbal medicine and pharmacognosy (the study of medicines of natural origin, usually from plants)—was an early trustee of ABC and the dean of the College of Pharmacy and Pharmaceutical Sciences at Purdue University and vice-president of academic affairs at Purdue.[6] He was the senior author of 6 editions of the leading textbook in the field, formerly used in every college of pharmacy in the United States.

Prof. Tyler urged his students and colleagues "not only to seek the truth but, after finding it, to discard any preconceived ideas which it may reveal as untrue;" encouraged scientific and product integrity; and envisioned a rational herbal healthcare sector that valued the proper evaluation of products' quality, safety, and efficacy.

According to Suter, Bioforce spends 4 to 5% of annual sales income on clinical research each year. The company's main focus is researching the effect that echinacea (*Echinacea* spp., Asteraceae) and saw palmetto (*Serenoa repens,* Arecaceae) have on common colds, infectious diseases of the upper respiratory tract, and benign prostatic hyperplasia, as well as herbal treatments for rheumatologic conditions and digestive disorders.

Bioforce has conducted at least 36 scientific studies on its products,[7] the majority of which were published in scientific, peer-reviewed journals (E. Sheets, e-mail, February 28, 2012). Fourteen of these studies were carried out on its flagship product, Echinaforce®, an organic tincture of *E. purpurea* herb and root that is used to treat colds and flu.[8] In 2006, an echinacea meta-analysis by Suter and fellow Bioforce AG scientist Roland Schoop was chosen as one of the top 25 research papers by the *Annual Bibliography of Significant Advances in Dietary Supplement Research*, published by the US National Institutes of Health Office of Dietary Supplements.[9]

Additionally, according to Bioforce USA's Managing Director Eileen Sheets, Bioforce's arnica (*Arnica* spp., Asteraceae) gel was the first product to obtain a traditional herbal registration from the United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA), and of the approximately 120 registrations that MHRA has granted, about a quarter of them have been given to Bioforce products.

"We are fascinated by medical plants and have an innate curiosity to find out how they act physiologically in a human being," said Suter. "Without [scientific] data, we could only rely on tradition, hearsay, or personal experiences; with these data we are credible and gain the trust of practitioners, pharmacists, and patients. Further, carrying out research allows us to find new indications for known plants and is one of the key drivers to stay innovative and successful. And last but not least, research carried out in phytotherapy helps the whole 'phytomedical' community, as we are living in times of evidence based medicine."

According to Bioforce USA President and CEO Pierce S. Sioussat, the acceptance of herbal medicine in the United States "can only be accomplished through continued investment in clinical research using commercially available products that are manufactured in a manner that ensures batch-after-batch and year-after-year consistency. It is also important that such research have a credible forum for public disclosure, and, in this regard, the American Botanical Council plays a critical role" (e-mail, February 28, 2012). Bioforce USA is a partner company that will accept the ABC award on Bioforce AG's behalf.

Bioforce AG's product integrity begins by honoring one of the most important philosophies of Swiss clinical herbalist Alfred Vogel, who founded the company in 1963: insisting that the plants used in its products are grown organically on its own farms or contract farms assessed for sustainability and approved by the company itself.[10] According to Bioforce, the company also harvests at "ideal" times, uses high-quality seed varieties, allows the plants to sufficiently mature "until they reach optimum potential," and mixes harvest batches in order to ensure consistent efficacy. Suter said that the company always uses the whole plant in its products—another of Vogel's most important founding philosophies—and processes the plants within 24 hours after harvest to guarantee a "full spectrum of all active ingredients." In addition, the World Health Organization recognizes Bioforce for producing its products according to pharmaceutical Good Manufacturing Practices (GMPs).[5]

"Alfred Vogel viewed nature as his guide and practiced a holistic approach to the use of plants," said Sioussat of Bioforce USA. "[Vogel said,] 'Every substance contained in a plant has purpose and significance. They complement each other and act as a whole.' What makes Bioforce unique is that these are not hollow words, but rather a philosophy that we are not afraid to put to rigorous examination in the most demanding environments." HG

References

1. Upton R, Graff A, Joliffe G, Länger R, and Williamson E. *American Herbal Pharamcopoeia: Botanical Pharmacognosy–Microscopic Characterization of Botanical Medicines*. Boca Raton, FL: CRC Press; 2011.
2. Dr. Bharat B. Aggarwal. M.D. Anderson Cancer Center website. Available at http://faculty.mdanderson.org/Bharat_Aggarwal/. Accessed February 20, 2012.
3. Aggarwal B. *Healing Spices: How to Use 50 Everyday and Exotic Spices to Boost Health and Beat Disease.* New York, New York: Sterling Publishing; 2011.
4. The Vietnam-Laos International Cooperative Biodiversity Group: goals. The University of Illinois College of Pharmacy website. Available at: www.uic.edu/pharmacy/depts/ICBG/goals.php. Accessed February 22, 2012
5. Schofield L. Bioforce: a brand built on science, ethics, sustainability and fresh plants. Available at: www.bioforceusa.com/articles/articles.php. Accessed February 20, 2012.
6. Blumenthal M. Varro E. Tyler: 1926 - 2001. *HerbalGram*. 2001;53:70.
7. Clinical studies. Bioforce Canada website. Available at: www.avogel.ca/avogelinstitute/en/Studies/Clinical_studies.php. Accessed February 28, 2012.
8. How Echinaforce is made. A. Vogel website. Available at: www.bioforceusa.com/home/Winter/how_echin_made.php. Accessed February 28, 2012.
9. NIH recognizes Bioforce echinacea research. Bioforce USA website. Available at: www.bioforceusa.com/latest-news/NIH.php. Accessed February 28, 2012.
10. The Bioforce Group: our products. A. Vogel website. Available at: www.avogel.com/com/company/products.php. Accessed February 27, 2012.

The Growing Industry of Medicinal Cannabis Analysis

Most patients in the District of Columbia and the 16 states that have approved medical marijuana do not know the quality or potency of the cannabis (*Cannabis* spp., Cannabaceae) they receive to treat their health conditions. Due to the absence of generally accepted quality control and assurance in the industry, laboratories often present inaccurate and inconsistent results to the public. Amounts of the herb's primary active ingredients like THC (tetrahydrocannabinol) and CBD (cannabidiol)—as well as levels of potential contaminants, such as pesticides and mycotoxins—are often unknown or imprecise. An increasing number of patients want consistency in their herbal medicinal products, however, and valid testing could bring the medicinal* cannabis industry greater legitimacy.

"The ability to ascertain potency and content of cannabis products sold in the dispensaries is critical if we are going to be able to allow patients to know what they are getting and for them to be able to re-access strains that are effective for them," said Donald Abrams, MD, an integrative oncologist who studies clinical cannabis at the University of California San Francisco, where he is chief of hematology/oncology at San Francisco General Hospital (e-mail, February 15, 2012).

That the state-based medicinal cannabis industry is surviving without broadly implemented quality control standards speaks to both its infancy and lack of regulation at the state and federal levels as a result of its Schedule I controlled substance status. Since it was removed from the *United States Pharmacopiea* in 1942, the quality control and assurance that came to be imposed on other food products and botanical medicines have been neglected for cannabis.

This is on the cusp of changing, however, as several nonprofits, research organizations, and trade groups have initiatives specifically focused on creating a more scientific and legitimate medicinal cannabis industry. The British Columbia Institute of Technology, for example, joined with TerraSphere Systems in late 2010 to develop "quality standards for botanical drugs, in particular government licensed medicinal *Cannabis sativa*."[1] Also in 2010, the US trade group American Herbal Products Association (AHPA) formed a Cannabis Committee with the goal of addressing hemp product commerce and agriculture, as well as "the emergence of medical cannabis as a legal product in numerous states."[2] "The AHPA Cannabis Committee intends to develop recommendations to regulators in states that allow use of medical cannabis," said AHPA President Michael McGuffin. "It is possible that these recommendations to regulators will include suggestions on best laboratory practice. The committee's work on this is just beginning so more specific details are not known at this time" (e-mail, April 10, 2012).

Additionally, the nonprofit American Herbal Pharmacopoeia (AHP) is currently developing a cannabis monograph under the direction of its Executive Director Roy Upton. As is typical of all AHP work, the cannabis monograph will provide industry with a variety of scientifically valid analytical methods used in the identification, purity, and quality assessment of cannabis and its crude products.

"There is a critical need for quality controls to be put in place in the cannabis industry," said Upton. "Those with commercial interests, including analytical labs, are jumping on the cannabis money bandwagon using unvalidated and/or inappropriate testing methodologies designed to give customers the answers they want to hear and promote a false sense of security. We see the same practices occurring in other sectors of the analytical labs industry and we hope the AHP monograph will help to correct some of this through greater transparency and methods validation" (e-mail, April 4, 2012).

The National Cannabis Industry Association (NCIA), a trade group in Washington, DC, has a current campaign aimed at helping to "develop and promote industry-wide standards and best practices."[3] And in February of 2012, 3 California labs—Steep Hill, Pure Analytics, and CW Analytical—founded the nonprofit Association of California Cannabis Laboratories (ACCL)[4] to establish best practices for the industry.[5] Both groups were created relatively recently and, aside from encouraging ethics and professionalism, have not yet taken concrete actions concerning validated standards and analytical methods.

In early 2011, an analysis of the testing practices of 10 anonymous cannabis labs found that "the precision and proficiency of a majority of cannabis testing labs compared favorably to other analytical testing industries," but the authors noted that some labs "reported results that deviated substantially from the average, with unacceptable deviations of more than 25% from the mean.[6,7] Three of the 10 labs performed unacceptably on half of the tests."

"Seven out of the 10 labs we looked at came up with reasonably consistent potency results," said Dale Gieringer, PhD, executive director of California NORML, a nonprofit that seeks to reform the state's marijuana laws (e-mail, March 20, 2012). "The ones that didn't had quality control problems; they either weren't professionally run, or were using poor methodology."[6,7]

Describing the state of most cannabis testing labs, William Clark, PhD—of the contract research organization Pure Naturals Certified, LLC—said, "Most labs lack the understanding of how to validate test methods. Without the proper testing and standardization, there will be no credibility with state and federal legislators. Today, many labs are in the business for the wrong reasons" (oral communication, April 10, 2012).

Dr. Clark is a natural products chemist with 15 years of experience in the herbal and dietary supplements business, having been involved extensively in the development and validation of analytical test methods for Centrum Herbals as well as NSF International's Dietary Supplement Certification Program. Pure Naturals Certified, based in Colorado, is in the beginning stages of establishing a lab that will isolate standards and validate testing methods for medicinal cannabis. Dr. Clark said he will soon meet and discuss this initiative with state legislators and the Colorado Department of Revenue, which enforces the state's medicinal cannabis laws and policies.

"[Standardization] is the piece [Colorado is] looking for to legitimize themselves with the feds," said Dr. Clark. "The reason the feds are focused on California is because their state regulations aren't as well-defined as those in Colorado."

Michelle Sexton, ND, a clinical cannabis researcher at Bastyr

* This article refers to cannabis used for medicinal purposes as "medicinal cannabis." Some organizations, such as AHPA and Pure Naturals Certified, prefer to use "medical cannabis." ABC acknowledges the various nomenclatures of this term.

CANNABIS UPDATE

University in Redmond, Washington, who owns her own cannabis testing business, suggested that concerned consumers ask about the lab's validation of methodology—such as, "Who did it and how was it done?"—as well as if the lab adheres to Good Laboratory Practices, has demonstrated complete separation of cannabinoids, which internal controls are in place to assure accuracy of results, and whether a "standard curve" is run with every sample set. If the owner or operator cannot provide the answers to these questions—or does not understand these questions—its analytical results may be questionable, she said (e-mail, April 3, 2012). (AHPA also provides a guidance document on its website to help consumers in choosing an analytical lab.[8])

Impact of Quality Cannabis Analysis

Why is it important that growers or dispensers invest in accurate analysis of their products? According to Dr. Sexton, it is a matter of public safety. "When much of the flowering top being sold is grown indoors, it is a target for fungal infection and pest infestation," she said. "The potential profit and cost of growing indoors then necessitates using chemical warfare to bring a crop to market. If you consider that there are legitimately ill patients accessing this medicine—such as patients with cancer, HIV, neurodegeneration, liver disorders, kidney dysfunction, and more—it is an imperative to hold those who grow and dispense cannabis as medicine to a high standard of quality control."

In addition, she continued, patients who have little tolerance or risk factors for some side-effects of THC may have distressing experiences from high-potency plant material, which a recent study reports is the trend rather than the exception.[9]

After obtaining an accurate analysis, a dispensary can label its products with potency content information, which Steve DeAngelo—executive director of Oakland's Harborside Health Clinic dispensary—said enables patients to "more effectively self-titrate their cannabis intake," and "identify a particular cannabinoid profile that works best for them, such as CBD-rich cannabis." "Without cannabinoid potency testing," he noted, "these patients would be unable to identify the CBD-rich medicine."

When conducting clinical research on any substance, including cannabis, it is essential to know and document the potency of the study material. The only legal source of cannabis for research in the United States, the National Institutes of Drug Abuse (NIDA)—which contracts the University of Mississippi to grow its cannabis—labels the container that holds the cannabis cigarettes.[10]

"I have generally trusted the government and not had product re-tested," said oncologist Dr. Abrams. "In fact, since you have to document the use of each cigarette in the research, sending one off to be confirmed might raise an eyebrow. NIDA cannabis is generally less than 7% THC with little or no CBD. For most of the studies I have done, we used their 3.5-3.9% THC cannabis."

Some labs offer bacteria, mold, and contaminants testing, which Dr. Abrams said is helpful. "I always recommend that my cancer patients shop for organic produce to avoid herbicides, pesticides, and fertilizers—chemicals that we don't really need to have in our bodies. I would assume the same should hold true for medicinal cannabis." (AHPA published a guideline on microbiology and mycotoxins in botanical products in 2003.[11])

Possibly raising into question the validity of all cannabis testing, a peer reviewer of this article noted that if the test is done on a cannabis bud different from the one the patient actually receives, the testing is "meaningless" because phytochemical content can range from plant-to-plant even if it is the same strain. Also, storage time can affect a cannabis sample's potency. "This is why it is important to [ensure] that adequate sampling of an entire harvest is performed," said Dr.


Marijuana *Cannabis sativa*.
Photo ©2012 Steven Foster

al cannabis organizations were able to successfully implement high-quality testing standards and operations, might the US government have more respect for the industry and decrease raids and shutdowns?

"Not at all!" responded Dr. Abrams, a sentiment voiced by the majority of this story's sources, including DeAngelo and Dr. Gieringer, who said, "it will take a top-down political decision by Congress and/or the President to change policy. This will happen only when there is enough public pressure for legalization."

Dr. Clark, however, passionately and respectfully disagreed. Instead of being activists for legalization, he said, the industry should be focused on establishing scientific standards for testing potency and purity of medicinal cannabis. He noted that this will enable researchers to weed out redundant and ineffective strains currently in commerce, focus on strains and cannabinoid profiles that are effective for certain conditions, and implement a similar NSF-like program to certify dispensaries and growers.

"This is exactly what is needed to help the federal government feel comfortable to make a change for the better, for everyone," he continued. "This opens the door for legislative change in Washington, DC." HG

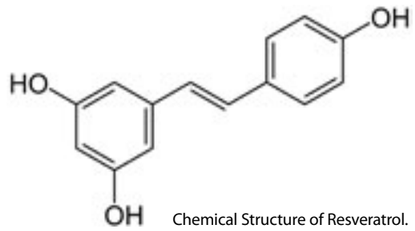
—Lindsay Stafford

References

1. Converted Organics announces agreement between the British Columbia Institute of Technology and TerraSphere to design a research approach for quality standards for medicinal plant products [press release]. Boston, MA: TerraSphere Systems. November 11, 2010.
2. Cosgrove J. The cannabis conundrum: AHPA tests the controversial waters with the formation of a Cannabis Committee. Nutraceuticals World. May 20, 2010. Available at: www.nutraceuticalsworld.com/contents/view_online-exclusives/2010-05-20/the-cannabis-conundrum/. Accessed April 4, 2012.
3. Campaigns. National Cannabis Industry Association website. Available at: http://thecannabisindustry.org/campaigns/#st. Accessed April 12, 2012.
4. For immediate release. Association of California Cannabis Labs website. Available at: www.cacannabislabs.com/. Accessed March 29, 2012.
5. The Association of California Cannabis Laboratories announces the establishment of a not-for-profit corporation [press release]. February 26, 2012. PRweb. Available at: www.prweb.com/releases/2012/2/prweb9226702.htm. Accessed March 28, 2012.
6. California NORML and Project CBD release the results of the first "Ring Test" to assess the accuracy of analytical laboratories [press release]. California NORML: San Francisco, CA. September 21, 2011. Available at: http://canorml.org/news/ringtest.html. Accessed March 26, 2012.
7. Gieringer D, Hazekamp A. How accurate is potency testing? *O'Shaughnessy's, the Journal of Cannabis in Clinical Practice*. Autumn 2011:17-18. Available at: http://projectcbd.com/RingTest.html#RingTest. Accessed March 26, 2012.
8. Dentali S. Choosing an analytical lab. *Natural Products Industry Insider*. September 15, 2003. Developed in cooperation with the Analytical Laboratories Committee of the American Herbal Products Association (AHPA). Available at: www.ahpa.org/Portals/0/pdfs/03_0915_NPI_Contract%20Lab.pdf. Accessed April 4, 2012.
9. Slade D, Chandra S, Mehmedic Z, et al. Potency trends of Δ9-THC and other cannabinoids in confiscated cannabis preparations from 1993 to 2008. *Journal of Forensic Sciences*. 2010;55:1209–1217.
10. Stafford L. The state of clinical cannabis research in the United States. *HerbalGram*. 2010;85:64-68.
11. Guidance on microbiology & mycotoxins. American Herbal Products Association website. Adopted June 2003; last revised November 2009. Available at: www.ahpa.org/Default.aspx?tabid=223#section_microbiology. Accessed April 4, 2012.

NIH Researchers Determine Resveratrol's Probable Health-Promoting Mechanism

Scientists have been studying resveratrol—a chemical that originates in grapes (*Vitis* spp., Vitaceae) and several other plants (*e.g.*, Japanese knotweed [*Polygonum cuspidatum*, Polygonaceae])—for its possible life-extending effects for about a decade, and have spent many more years studying its other potential health benefits. Inching toward household familiarity, research on the substance has even inspired American fiction, a memorable example being the short, comical chronicle of a wine-lapping lab rodent, "Mouse au Vin," that ran in a late-2009 issue of *The New Yorker*.[1]



Chemical Structure of Resveratrol.

Up until the present, though, resveratrol's precise mechanism of action has eluded experts. It was widely held that resveratrol promoted health by directly activating a protein related to caloric restriction called sirtuin 1, but debate persisted in the scientific community as studies generated varying results. (Unfortunately, an oeuvre of resveratrol journal articles by the director of the University of Connecticut's Cardiovascular Research Center, Dipak K. Das, PhD, describing the chemical's positive effects was recently reported to be riddled with false or fabricated data, causing some to question the veracity of resveratrol's reported benefits).[2]

A new study may put to bed conjecture over resveratrol's means of imbuing positive health effects. On February 2, 2012, the US National Institutes of Health (NIH) issued a press release stating that its researchers had pinpointed the probable mechanism of action by which resveratrol promotes health, knowledge that also may be useful in creating new approaches for treating heart disease, type 2 diabetes, and Alzheimer's disease.[3]

Principle study author—and Chief of the Laboratory of Obesity and Aging Research at NIH's National Heart, Lung, and Blood Institute—Jay H. Chung, MD, PhD, has been researching resveratrol for 5 years. "It captivated my interest because a simple, naturally occurring compound was able to mimic certain healthful aspects of calorie restriction," he said (e-mail, February 17, 2012).

Dr. Chung and the co-authors of the NIH study, which was published in the journal *Cell*, "present evidence that resveratrol does not directly activate sirtuin 1, a protein associated with aging," debunking conclusions from a number of preceding studies.[3] Indeed, according to the study authors, "resveratrol inhibits certain types of proteins known as phosphodiesterases (PDEs), enzymes that help regulate cell energy."[3]

Chung *et al*. confirmed in an early experiment that resveratrol could not be interacting directly with sirtuin 1—previously postulated by Pacholec *et al.* in 2010[4]—because "resveratrol activity required another protein called AMPK." (AMPK is the acronym for an enzyme known as 5' AMP-activated protein kinase.) By observing metabolic activity in resveratrol-treated cells, the scientists discovered that the protein PDE4 is inhibited by resveratrol. This inhibition starts a chain reaction that activates AMPK, which leads to the activation of sirtuin 1 along the way.

"There was doubt about previous studies' conclusions before we entered the picture," said Dr. Chung, "We suspected AMPK may be involved because activation of AMPK leads to the benefits that are very similar to those of resveratrol. When we discovered that the metabolic effects of resveratrol disappear without AMPK, we knew that AMPK was the principal player in resveratrol action."

The researchers tested their hypothesis by dosing mice with a drug called rolipram, which also inhibits PDE4, and the positive health benefits were identical to those associated with resveratrol, such as "preventing diet-induced obesity, improving glucose tolerance, and increasing physical endurance."[3]

(FDA has approved roflumilast [marketed as Daliresp® by Forest Pharmaceuticals, Inc., and Daxas® by Nycomed], another drug that inhibits PDE4, for the treatment of obstructive pulmonary disease.)[3]

While the conclusions of the study represent a step forward in resveratrol research, they also reveal a more complex chemical than previous studies have shown. According to Dr. Chung, natural resveratrol affects many non-PDE proteins, and because of that, high doses of resveratrol such as those used in human clinical studies (1 gram/day, equivalent to 667 bottles of red wine) "may cause not-yet-known toxicities as a medicine, particularly with long-term use."[3]

"No one has done a good long-term study, either in animals or in humans, on the potential toxicities of resveratrol… At this point," said Dr. Chung, "we don't know enough to predict what types of toxicities may exist, if at all."

Equipped with the data yielded from the rolipram study, Dr. Chung intends to follow it up with a clinical trial.

"We will be testing PDE4 inhibitors in obese individuals at risk for developing type 2 diabetes," he said "[to] determine whether it can improve insulin sensitivity." HG

—Ashley Lindstrom

References

1. Baumbach N. Mouse au vin. *The New Yorker*. January 26, 2009. Available at: www.newyorker.com/humor/2009/01/26/090126sh_shouts_baumbach#ixzz1mOJBtYzT. Accessed February 17, 2012.
2. Wade N. University suspects fraud by a researcher who studied resveratrol. *The New York Times*. January 11, 2012. Available at: www.nytimes.com/2012/01/12/science/fraud-charges-for-dipak-k-das-a-university-of-connecticut-researcher.html. Accessed February 14, 2012.
3. NIH study uncovers probable mechanism underlying resveratrol activity [press release]. National Institutes of Health News. February 2, 2012. Available at: www.nih.gov/news/health/feb2012/nhlbi-02.htm. Accessed February 3, 2012.
4. Pacholec M, Chrunyk B, Cunningham D, et al. SRT1720, SRT2183, SRT1460, and resveratrol are not direct activators of SIRT1. *J Biol Chem* 2010;285:8340–8351. Available at: www.jbc.org/content/285/11/8340. Accessed February 17, 2012.

Multi-Center Consortiums Seek to Create Better Plant Medicines

Two multi-institutional consortiums funded by the US National Institutes of Health (NIH) have mapped the genes of dozens of medicinal plants in order to study how they create complex therapeutic compounds. Using this genetic data, the researchers plan to engineer plants to produce more of a specific naturally occurring medicinal chemicals, or slight variations of these phytochemicals, which they hope will result in new and better medicines.[1]

The Medicinal Plant Consortium (MPC) and the Medicinal Plant/Human Health Consortium (MP/HHC)—2 separate but similar projects—are funded by grants totaling about $9 million, awarded by the National Institute of General Medical Sciences at NIH and made possible by the American Recovery and Reinvestment Act.[1,2] The MPC team is led by the University of Kentucky (UK) and also includes Iowa State University, Michigan State University, the University of Mississippi, Purdue University, Texas A&M University, and the John Innes Centre in Norwich, England. The MP/HHC is led by Washington State University (WSU), and has partnered with the Dorothy Bradley Atkins Medicinal Plants Garden of the University of Illinois at Chicago (UIC), the Donald Danforth Plant Science Center in St. Louis, and the National Center for Genome Resources in Santa Fe, New Mexico.[2]

MPC leader and UK plant science professor Joe Chappell, PhD, said the MPC's work would not have been possible without the people at each of the participating institutions who had a particular interest in one or more of the target plants. "This is what made our efforts so rich. We had expertise for each of the identified plants, propagating the plant, and knowing a lot about where and how to look for interesting compounds in the plants" (e-mail, January 5-10, 2012).

Both consortiums started their work in 2009 by obtaining physical specimens. Norman G. Lewis, PhD, leader of the MP/HHC and Regents Professor and Director at WSU, emphasized that their team of experts in medicinal plant biochemical pathways carefully selected species with the most complex chemical structures, as well as those widely used in medicine today. "Many of the plants being studied are not only medicinally useful, but their molecules are structurally complex and it is therefore very expensive and difficult to synthesize them," said Dr. Lewis (oral communication, January 17, 2012). Because many of the plants are over-harvested and even endangered in their native lands, the consortiums hope to engineer alternative plants and plants in cell culture in order to reduce the threat of species extinction.

Herbs analyzed by the consortiums include ginseng (*Panax* spp., Araliaceae), andrographis (*Andrographis paniculata*, Acanthaceae), marijuana (*Cannabis sativa*, Cannabaceae), hoodia (*Hoodia gordonii*, Apocynaceae), ginkgo (*Ginkgo biloba*, Ginkgoaceae), foxglove (*Digitalis purpurea*, Scrophulariaceae)—the source of the widely used heart drug digoxin—and periwinkle (*Catharanthus roseus*, Apocynaceae), which is used to make medicines that treat several cancers, childhood leukemia, and Hodgkin's disease. Dr. Lewis pointed out that the medicinal plants chosen include those extensively used in pain management, such as morphine from the opium poppy (*Papaver somniferum*, Papaveraceae); cancer treatment, such as *Taxus* species harboring the anti-cancer compound paclitaxel (Taxol®), podophyllotoxin from Himalayan mayapple (*Podophyllum hexandrum*, Berberidaceae), and camptothecin from *Camptotheca acuminata* (Cornaceae); and others in consideration for disorders such as for Alzheimer's disease and new cancer treatments.

Using almost any plant tissue, the consortium researchers were able to sequence the genes expressed throughout each plant, resulting in sets of data called transcriptomes. A transcriptome is not an entire genome, but a small subset of genome DNA comprised of "all the genes that are important for creating the individual plants," said Dr. Chappell. Researchers can use the transcriptomes to look for the genes that are "switched on" and "sending messages" throughout the plant—which indicates that an important substance or process is being activated—and then reassemble these "candidate" genes using algorithms, said Dr. Lewis.

For example, scientists know that valerian (*Valeriana officinalis*, Valerianaceae) produces several different kinds of chemicals, but have not determined which is responsible for the plant's sedative effects. According to Dr. Chappell, MPC's work has generated information that will help them identify valerian plant lines or tissues where one or more of these compounds might accumulate. These genetic maps provide insight into how plants biosynthesize or assemble molecules to make complex and medicinal compounds. The researchers will also be able to produce the compounds and derivatives in alternative organisms.

"We should be able to create a yeast line that produces one of the active ingredients of the *Valeriana* plant," said Dr. Chappell. "I know this sounds crazy, but it's terribly exciting—if we can isolate one active ingredient, then we can probably make a few changes to the compound and possibly make it a more effective medicinal. We are trying to glean the secrets plants learned [throughout evolution] that allowed them to make fantastic chemicals, chemicals that gave plants the adaptive advantages to live in all kinds of habitats on planet earth, and

Scientists also could create potentially better medicines by modifying the medicinal compounds. "Very often," said Dr. Lewis, "plants make a chemical structure or scaffold that can be modified chemically upon and improved. Once you change or modify a compound with parts of other molecules it can affect the mode of action, and take it away from being, for example, very toxic or not very effective to being a blockbuster drug."

chemicals that man has learned to use for our own purposes (food, medicines, etc)."

Scientists also could create potentially better medicines by modifying the medicinal compounds. "Very often," said Dr. Lewis, "plants make a chemical structure or scaffold that can be modified chemically upon and improved. Once you change or modify a compound with parts of other molecules it can affect the mode of action, and take it away from being, for example, very toxic or not very effective to being a blockbuster drug."

The MPC made its transcriptomes available online in December of 2011, and MP/HHC has made most of the transcriptomes available, though it is waiting to obtain a couple of rare plants from places like Indonesia. Dr. Chappell said researchers and industry members around the globe are already taking advantage of the information. "You may know that the nutraceuticals industry wants to have higher standards for their products. So the manufacturers of supplements are using our information to develop better quality control standards for their products. One example of this technology is DNA barcodes, little technology tags that can be used by the manufactures to document what plant species are actually in their product and to inform the customer if any other plant materials (*i.e.*, contaminants) might also be in the product."

The consortiums' members are now working on mapping the plants' metabolomes and publishing them online. Metabolomes are "like a fingerprint of all the molecules that are in the plant," said Dr. Lewis. Though previous work has been done in this area, Dr. Lewis noted that the progress has been limited due to the years of dedicated research it takes to identify each step in a biochemical pathway. According to UIC's webpage for the MP/HHC, "The current understanding of the formation of plant-derived medicinal compounds at the enzyme, gene, and regulatory levels is very incomplete. Not a single complex plant medicinal pathway has yet to be completely elucidated at both the enzyme and the regulatory level."[3]

"But with this consortium work," said Dr. Lewis, "one has the expectation that one can identify the genes much faster. We've basically opened up a treasure trove of information."

More information on MPC is available at http://medicinalplantgenomics.msu.edu and http://metnetdb.org/mpmr_public/. More information on MP/HHC is available at www.uic.edu/pharmacy/MedPlTranscriptome. HG

—Lindsay Stafford

References

1. New light on medicinal benefits of plants. Science Daily. December 15, 2011. Available at: www.sciencedaily.com/releases/2011/12/111215095243.htm. Accessed January 9, 2012.
2. Welcome to our website. Transcriptome Characterization, Sequencing, And Assembly Of Medicinal Plants Relevant To Human Health website. Available at: www.uic.edu/pharmacy/MedPlTranscriptome/#. Accessed January 9, 2012.
3. Soejarto S. Why the transcriptome project? Transcriptome Characterization, Sequencing, And Assembly Of Medicinal Plants Relevant To Human Health website. June 18, 2011. Available at: www.uic.edu/pharmacy/MedPlTranscriptome/about.html. Accessed January 9, 2012.

American Herbal Pharmacopoeia Releases New Monographs on American Ginseng Root and Slippery Elm Inner Bark

In 2011, the nonprofit American Herbal Pharmacopoeia (AHP) produced new monograph standards and therapeutic compendia for American ginseng root (*Panax quinquefolius*, Araliaceae) and slippery elm inner bark (*Ulmus rubra*, Ulmaceae). Each guide serves as an authoritative standard for verifying its corresponding herb's proper identity and purity, as well as for establishing quality and composition guidelines to be used for fulfilling Good Manufacturing Practice (GMP) requirements. The therapeutic compendium provides a comprehensive review of current pharmacological and safety data and contains information on toxicology, medical indications, structure-function claims, dosages, interactions, side effects, and more.[1] This information is essential for manufacturers who need to maintain safety and efficacy documentation that supports their products and claims.

AHP began producing monograph standards and therapeutic compendia in 1994 for some of the most commonly used botanicals used in Ayurvedic, Chinese, and Western herbal medicine. The first full AHP monograph—on St. John's wort (*Hypericum perforatum,* Clusiaceae)—was published in 1997 as a special insert in *HerbalGram* #40. According to its website, AHP monographs "provide standards, guidance, and validated methods needed for all aspects of botanical identification and quality control."[1] The recently released American ginseng root and slippery elm inner bark monographs bring the total number of AHP monographs to 32.

American Ginseng Root

AHP Executive Director Roy Upton described cultivated American ginseng as "one of the most widely adulterated herbs" in the Western herb market in a December 2011 press release.[2] "We have found leaf material marketed as root, exhausted marc being sold as crude root, and materials cut with 45% dicalcium phosphate," he said. "The monograph provides all the characterizations that any quality control team requires for making an authentic and quality product." ("Marc" refers to the remaining inert herbal material [mainly fibers and/or starch] after all or most phytochemicals have been extracted with a solvent.)

Preparations from cultivated American ginseng have been used traditionally to support the immune system, strengthen the nervous system, and to help prevent certain chronic conditions. Research on American ginseng has focused on blood sugar control for type 2 diabetes and quality of life in cancer patients. A patented, chemically defined (polysaccharide-based) extract made from cultivated American ginseng roots has shown efficacy in helping to prevent and treat upper respiratory tract symptoms related to colds and flu.[3]

Upton said consumers should be aware of potentially adulterated products when shopping for American ginseng supplements. "If it is cheap, then it is because cheap ingredients were used," he said (e-mail, February 14-20, 2012). "If you open a capsule and it is gritty, it may contain a large amount of flow agent or filler (*e.g.*, magnesium stearate)."

For almost 40 years, wild American ginseng has been protected under an international treaty known as the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES). The treaty requires the US Fish and Wildlife Service (FWS) to regulate the wild herb's export and to ensure that it is harvested in a sustainable manner.[4] According to a 2011 FWS report, the main threats to wild American ginseng are illegal harvest, irresponsible harvest, consumption by white tail deer, invasive plant species, and habitat loss and destruction.[5]

The American Herbal Products Association (AHPA), the leading trade association dealing with herbs in the United States, released good stewardship practices for wild American ginseng in 2006.[6] The same year, FWS reverted to a 5-year age minimum for harvesting wild American ginseng—half that of the 10-year minimum briefly established in 2005—after receiving feedback from growers, harvesters, and other industry representatives.[4] AHPA's good stewardship brochure includes information on the plant's life cycle, obtaining permission to harvest, and how and when to sustainably harvest the herb.

Wild American ginseng can be found in 34 states, but only nineteen are permitted by FWS to export the herb. In 2010, the total harvest of wild American ginseng was 32 tons, approximately 10 tons less than the amount harvested in 2009—the largest annual harvest since 1997.[5] AHPA reports that the biggest markets for wild American ginseng are Asian countries, which import roughly 30 tons of the herb every year.[6]

Wisconsin, in particular, is known for its high-quality cultivated American ginseng. During the last 20 years, Wisconsin farmers have struggled to keep up with international competition—especially from Canada and China—and manufacturers that falsely claim their American ginseng is Wisconsin-grown. In 1991, the Ginseng Board of Wisconsin, a nonprofit organization representing Wisconsin ginseng farmers, created the Wisconsin Ginseng Seal Program to identify products that contain 100% pure and authentic Wisconsin-grown ginseng roots.[7]

Slippery Elm Inner Bark

AHP announced the release of monograph standards and a therapeutic compendium for slippery elm inner bark in March 2011. This popular botanical native to America is commonly found in throat lozenges (e.g., Thayers®; Henry Thayer Co., Westport, Connecticut) and herbal teas (e.g., Throat Coat®; Traditional Medicinals, Sebastopol, California; and Essiac®; Essiac Canada International, Quebec, Canada). Slippery elm is one of the few herbs approved by the US Food and Drug Administration (FDA) as a safe and effective nonprescription drug ingredient that can be sold over-the-counter (OTC) as a demulcent for soothing sore throats.[8]

Upton explained some of the reasons for FDA's approval of slippery elm as a botanical drug. "It was originally grandfathered in as an 'old drug,'" he said. "Then, when FDA was reviewing 'old drugs,' Thayers—who was the first to introduce the lozenge historically and [had] the primary interest in slippery elm lozenges—was there to provide FDA with enough data to maintain the classification."

Other botanicals, Upton continued, have not been approved by FDA as non-prescription drugs because of the prohibitively high cost. "It now costs approximately $750 million to prove a drug is safe and effective," he said. "No one will do that for chamomile tea."

In addition to sore throat relief, slippery elm has been used traditionally as a topical treatment for healing wounds and skin diseases and internally to treat inflammation of the digestive, respiratory, and urinary systems. According to the AHP Therapeutic Compendium, slippery elm was also one of the most widely used nutritive herbs historically, with reports of Civil War soldiers subsisting on the bark of slippery elm for weeks, demonstrating the plant's nutritive as well as medicinal qualities.[8] Further, according to the National Geographic's *Guide to Medicinal Herbs*, George Washington and his troops reportedly survived for 12 days at Valley Forge on slippery elm porridge during the American Revolution. The porridge, with a nutritional content similar to that of oatmeal, can be made from ground inner bark and water or milk.[9]

In recent years, illegal stripping of slippery elm trees has been reported in some national forests in the United States. However, the modest price of slippery elm has prevented it from becoming a widespread problem among illegal harvesters. More serious threats to the tree include land development, logging, and habitat depletion.[10]

AHP chose to review slippery elm inner bark, in part, because of its popularity and occasional quality control issues. "There are significant quality issues associated with slippery elm, including supplies—which are impacted by Dutch elm disease—and poor quality material ([*e.g.*,] not meeting swelling index-mucilage values)," Upton explained, referring to the quality of the slippery, viscous fluid extracted from the tree's inner bark.

One of the main goals of AHP's monographs is to ensure consumer access to high-quality herbal materials. "As mandated by current and future [GMPs], the fields of information [in the monographs] provide industry with a scientifically valid means to ensure the authenticity, purity, and quality of botanical ingredients and dietary supplements," AHP states on its website.[1]

Today, the FDA-approved botanical ingredient can be found in many herbal throat lozenges and is commonly sold in drug stores. "Slippery elm lozenge has been a very important preparation for generations," said Upton.

The American ginseng root and slippery elm inner bark monographs are available through AHP's website. PDF copies are available for $39.95 each and hard copies can be purchased for $44.95 each. For more information, visit www.herbal-ahp.org. HG

—Tyler Smith

References

1. AHP monographs. American Herbal Pharmacopoeia website. Available at: www.herbal-ahp.org/documents/newsroom/AHP_Monographs.pdf. Accessed February 24, 2012.
2. AHP releases monograph standards and therapeutic compendium for *American Ginseng* root (*Panax quinquefolius* L.) [press release]. Scott's Valley, CA: American Herbal Pharmacopoeia. December 7, 2011. Available at: www.herbal-ahp.org/documents/press_releases/American%20Ginseng%20PR%20final.pdf. Accessed February 20, 2011.
3. American ginseng. University of Maryland website. Available at: www.umm.edu/ altmed/articles/american-ginseng-000248.htm. Accessed February 20, 2011.
4. Cavaliere C. U.S. FWS reinstates 5-year age limit for exported wild American ginseng. HerbalEGram. 2006;3.
5. Gnam R. Advice for the export of roots of wild and wild-simulated American ginseng (*Panax quinquefolius*) lawfully harvested during the 2011 harvest season in 19 states. Washington, D.C.: US Fish and Wildlife Service; 2011.
6. Good stewardship harvesting of wild American ginseng (*Panax quinquefolius*). US Fish and Wildlife Service website. Available at: www.fws.gov/international/DMA_DSA/CITES/ pdf/2010wild-simulatedginseng.pdf. Accessed February 22, 2011.
7. Wisconsin ginseng farmers fight to protect product reputation. *HerbalGram*. 2007. 75:54-61.
8. AHP releases monograph standards and therapeutic compendium on slippery elm (*Ulmus rubra* Muhl.) inner bark [press release]. Scott's Valley, CA: American Herbal Pharmacopoeia. March 10, 2011. Available at: www.herbal-ahp.org/documents/press_releases/Slippery%20elm%20press%20release.pdf. Accessed February 22, 2011.
9. Johnson RL, Foster S, Low Dog T, and Kiefer D. *National Geographic Guide to Medicinal Herbs: The World's Most Effective Healing Plants.* 2011: National Geographic Press; Washington, D.C.
10. Cavaliere C. Illegal stripping and conservation of slippery elm trees. *HerbalGra*m. 74:54-61. Available at: http://cms.herbalgram.org/herbalgram/issue74/article3123.html.

New Hope Natural Media Inducts Honorees into 'Hall of Legends'

Thirteen esteemed individuals from various sectors of the natural products industry were inducted into the New Hope Natural Media Hall of Legends at the first annual ceremony in Anaheim, California, on March 8, 2012. The event took place in conjunction with the NutraCon's NutrAward reception at Natural Products Expo West/Engredea. Engredea, like Expo West, is an annual event that showcases product innovations in the natural food, beverage, dietary supplement, and cosmetic industries.

"There are a lot of lifetime achievement awards; there are a lot of champion awards, but there's no singular place where all of the people who have created this industry are co-recognized," said Len Monheit, the executive director of Engredea (oral communication, March 20, 2012). "So there was an opportunity to create a Hall of Fame, a Hall of Legends, which didn't exist, gather those individuals and their contributions and help educate newer folks in the industry about where the industry has come from."

When narrowing down the list of potential Legends, Monheit and his colleagues at New Hope considered individuals from vastly different backgrounds. "We determined that it needed to cover the entire industry and it needed to be anyone that has impacted this industry that we get our livelihoods from and have such passion for," said Monheit. "We really tried to make it a rounded group."

Honorees include the following individuals:[1]

- Jeffrey S. Bland, PhD, chief science officer of Metagenics
- Mark Blumenthal, founder and executive director of the American Botanical Council (ABC)
- John Carlson, PhD, co-founder of the nutritional supplement company JR Carlson Labs, who passed away in October 2011
- Steve Demos, founder of WhiteWave Foods (makers of Silk® soymilk products, now part of Dean Foods) and NextFoods
- Annette Dickinson, PhD, president of Dickinson Consulting, LLC, and former president of the Council for Responsible Nutrition, a leading industry trade association
- Norman R. Farnsworth, PhD, internationally respected pharmacognosist at the University of Illinois-Chicago and co-founder of ABC, who passed away in September 2011
- Michael Funk, chair and co-founder of United Natural Foods, Inc., the largest wholesale distributor of natural foods and dietary supplements to natural food stores and grocery stores
- Sandy Gooch, founder of Mrs. Gooch's, an early, pioneering chain of natural grocery stores in the Los Angeles area (purchased by Whole Foods Market)
- Gary Hirshberg, co-founder of Stonyfield Farm, the world's leading producer of organic yogurt
- Loren Israelsen, executive director of the United Natural Products Alliance and a key architect of the Dietary Supplement Health and Education Act of 1994
- Bob MacLeod and Steve Byckiewicz, founders of Kiss My Face, a pioneering natural cosmetics company
- Elwood Richard, founder of NOW Foods

As part of the ceremony's educational mission, a mobile "Hall of Legends" will be on display at all New Hope expos and events.

"I've been very, very fortunate to know some of these people, but there are a lot of new people in this industry that don't know the evolution and the commitment and the passion that has created the opportunity for us to work in this industry," said Monheit.

Despite their varied backgrounds, the 13 inductees are united in their passion for the natural products industry. "[What they have in common] is a desire to do good; a desire to build something: greater health, more sustainability," Monheit continued. "[It's] a commitment right from the core of the person."

"All of us are doing what we want to do," said Blumenthal. "We are following our own bliss, creating our own paths, making up the rules as we move forward. It is a true gift and privilege to be able to be your own boss doing something that is new and different."

Monheit described the atmosphere in Anaheim for the inaugural ceremony. "Watching and listening to the response of the crowd and the excitement and the energy … was astounding and very rewarding," he said. "I think you could feel the passion; I think that the people who had a hint of what this industry [is] about came away with much more of a connection to its origins and to its spirit and commitment." HG

Source

1. Hall of Legends 2012 honorees. New Hope 360 website. Available at: http://newhope360.com/tradeshows/hall-legends-2012-honorees. Accessed March 26, 2012.

Researchers Conduct Survey of Wild Chinese Herbs on Rural Tibetan Plateau

Researchers recently completed a 6-year effort in which they documented more than 1,000 wild herbs in the Sanjiangyuan National Nature Reserve on the Tibetan plateau in Qinghai Province, China. The scientists identified 575 varieties of medicinal herbs—six of which were previously unknown to the area—and captured more than 100,000 photographs of local flora.[1] The Sanjiangyuan region (translated as "Three Rivers' Source") comprises the headwaters of the Yellow, Yangtze, and Mekong Rivers. The greater Tibetan plateau has been described as the "Third Pole" or the "Roof of the Earth" in terms of ecological importance.[2]

The multi-year survey is part of a strategy of the Chinese government to protect and conserve the fragile region, which in recent years has been impacted negatively by climate change and excessive herding.[1] The wild herb conservation project is one aspect of China's Great Western Development Strategy, an initiative that took effect in 2005 to improve less-developed regions in rural western China.[3] In 2011, China invested 1 billion yuan (approximately $160 million USD) to protect the environment of the Sanjiangyuan region, according to an article from *China Daily*.[4]

As part of the development plan, "[The Chinese Academy of Sciences] will select … species with promising potential and significant research value, especially plants that are important in the agricultural, pharmaceutical, and industrial fields and that could be put into industrial production," the organization mentions on its website. "Together with the ongoing drive to standardize medicinal herbs in Chinese traditional medicine [and] comprehensively utilize Tibetan traditional medicine, … the academy will make efforts to find drugs that are highly effective against major diseases."[3]

Yuntao Zhao, Senior Program Officer at the World Wide Fund for Nature (WWF)-China, described the 6 species not previously known in the Sanjiangyuan region (e-mail, January 28, 2012). The species include the following plants: *Corydalis boweri* (Papaveraceae), *C. hendersonii*, *C. tianzhuensis*, *Meconopsis henrici* (Papaveraceae), *Phlomis younghusbandii* (Lamiaceae), and *Lloydia tibetica* (Liliaceae).

According to Sir Ghillean Prance, the former director of the Royal Botanic Gardens at Kew, these plants are not newly discovered species (e-mail, January 28, 2012). Records of these plants have existed for years, just not in the protected Sanjiangyuan region. "The [plants were] described long ago," he said. "For example, *Phlomis younghusbandii* in 1938, *Lloydia tibetica* in 1892, and *Meconopsis henrici* in 1896."

Despite the extreme climate and isolated location, a population of roughly 200,000 people, most of whom are Tibetan herders, inhabit the reserve—the second largest nature sanctuary in the world.[5] Noted botanist, photographer, and author Steven Foster explained that traditional medicinal plants used by inhabitants of the Tibetan plateau can vary greatly.

"These areas have the largest numbers of [Chinese] ethnic minorities, all of whom have their own folk medicine traditions," said Foster (e-mail, January 30, 2012). "Tibetan medicine would not be practiced by nomadic Tibetan herders, whose medicine is more of a localized folk medicine practice; nothing as formal as Tibetan medicine (though similar concepts and plants may be employed)."

According to a February 4, 2012 article in *The Economist,* "In recent years, rural incomes in eastern areas of the vast Tibetan plateau have been soaring thanks to a demand for Tibetan herbal remedies."[6]

Despite the encouraging outlook for certain medicinal herbs in China, Dr. Prance explained that high demand could lead to disastrous consequences. "When the use of medicinal plants is encouraged, the danger is overuse, especially of local plants with small populations," he said. "Many medicinal plants are now severely threatened species."

Foster believes that existing conservation laws are likely not enough to solve the problem.

"The Sanjiangyuan National Nature Reserve, like most natural reserves, discourages harvest of biota; though in most places in the world, such rules or laws are rarely enforced," said Foster. "Conservation only has teeth, so to speak, when it involves the trade of endangered animals. Plants don't have cute little brown eyes or soft fur, so they garner little conservation attention and much less enforcement of existing rules and laws." HG

—Tyler Smith

References

1. Hong'e M. China completes field research of wild herbs in Sanjiangyuan. Xinhua News Agency website. Available at: http://news.xinhuanet.com/english/china/2012-01/25/c_131376710.htm. Accessed January 25, 2012.
2. Li XL, Brierley G, Shi DJ, Xie YL, Sun HQ. Ecological Protection and Restoration in Sanjiangyuan National Nature Reserve, Qinghai Province, China. In: Higgitt D (ed.). *Perspectives on Environmental Management and Technology in Asian River Basins.* Dordrecht Heidelberg New York: Springer. 2012;93-120 [Abstract].
3. An Outline of the CAS Action Plan for the Development of Western China. Chinese Academy of Sciences website. Available at: http://english.cas.cn/ST/BR/br_rp/200909/t20090914_37780.shtml. Accessed January 31, 2012.
4. China spends $158m protecting major riverheads. China Daily website. Available at: www.chinadaily.com.cn/china/2012-01/23/content_14490535.htm. Accessed January 25, 2012.
5. Sanjiangyuan (Three Rivers' Headwaters) National Nature Reserve (SNNR). Plateau Perspectives website. Available at: www.plateauperspectives.org/sanjiangyuan.htm. Accessed January 26, 2012.
6. No power to pacify: more discontent on the plateau, despite strong economic growth. *The Economist* website. Available at: www.economist.com/node/21546058. Accessed February 2, 2012.

Curcumin Studied for Prevention of Colorectal Neoplasia

Reviewed: Carroll RE, Benya RV, Turgeon DK, *et al.* Phase IIa clinical trial of curcumin for the prevention of colorectal neoplasia. *Cancer Prev Res* (Phila). 2011;4(3):354-364.

Curcumin is a biologically active compound derived from turmeric (*Curcuma longa*, Zingiberaceae) root and has anti-inflammatory, antioxidant, and antineoplastic activity (preventing the growth of benign or malignant cancerous cells). The effects of curcumin on colorectal abnormal tissue development (called crypt foci) in humans have not been previously reported. Tobacco smokers develop more aberrant crypt foci—tube-like structures in the colon and rectum that are the precursors to polyps and colon cancer. The authors of this trial hypothesize that if curcumin could reduce the concentration of the eicosanoids prostaglandin E_2 (PGE_2) and 5-hydroxyeicosatetraenoic acid (5-HETE) in the colorectal lining, it could reduce the formation of aberrant crypt foci. The purpose of this phase IIa cancer prevention study was to measure the effects of oral curcumin on PGE_2 and 5-HETE concentrations within aberrant crypt foci and on the number of aberrant crypt foci and their proliferation in an open-label, non-randomized study.

Turmeric *Curcuma longa.* Photo ©2012 Steven Foster

Participants were recruited from the University of Illinois at Chicago and the Colorectal Screening Clinic at the University of Michigan, Ann Arbor, Michigan. Eligible subjects were men or women who were currently smokers, aged 40 years or more, with a history of more than 3 pack-years (a participant who smoked at least 1 pack of cigarettes per day for 3 years), and 8 or more rectal aberrant crypt foci observed via magnification chromoendoscopy (colonoscopy). Excluded subjects were those who used nonsteroidal anti-inflammatory drugs for more than 10 days per month, unless they completed a 30-day washout period, or had a history of chronic inflammatory bowel disease, prior pelvic irradiation, or an endoscopically confirmed peptic ulcer within the previous 5 years. Subjects were treated for 30 days with 2 g/day (n=22) or 4 g/day (n=19) curcumin (micronized and provided by the National Cancer Institute's Division of Cancer Prevention; Bethesda, Maryland). Biopsies of aberrant crypt foci and normal rectal mucosa were taken at baseline and post-treatment; and PGE_2 and 5-HETE were measured, and crypt cell proliferation was evaluated. Blood was drawn to assess plasma curcumin levels. A post-treatment endoscopic examination was performed between day 30 and day 35, and curcumin was continued until the day of the exam to ensure that biopsies were obtained less than 4 hours postdose. All laboratory assessments were evaluated blindly. Treatment adherence was measured via phone call, patient diary, and pill count.

Both doses of curcumin did not significantly change PGE_2 or 5-HETE concentrations between baseline and post-treatment in the normal mucosa or mucosa with aberrant crypt foci. The 2 g dose of curcumin did not alter the number of aberrant crypt foci between baseline and post-treatment. In contrast, however, the 4 g dose of curcumin significantly decreased the number of rectal aberrant crypt foci by 40% from baseline to post-treatment (17.8 vs. 11.1 foci, $P<0.005$). However, there was no corresponding decrease in Ki-67-detected mucosal proliferation. Only low levels of curcumin and its conjugates were detected in rectal mucosal biopsies. After treatment with 4 g of curcumin (but not 2 g curcumin), plasma levels of curcumin conjugate concentrations were significantly elevated ($P=0.009$). Both doses of curcumin were well tolerated. The most frequently reported adverse events were gastrointestinal disturbances (diarrhea, distention, and reflux).

The authors conclude that the 4 g dose of curcumin significantly reduced aberrant crypt foci formation, which is an important anticarcinogenic effect. The mechanism remains undetermined. The curcumin-induced reduction in aberrant crypt foci occurred via a systemic rather than a local effect. It is interesting that the anticarcinogenic activity occurred at the target tissue despite the lack of curcumin detected in the target tissue.

It should be noted that the subjects had to take 16 curcumin capsules/day to attain a 4 g dose. It is well known that patient compliance is low when numerous capsules have to be consumed. Therefore, it is possible that for this to be a viable anticancer option, the product should either be more concentrated (a difficult task with a pure compound like curcumin) or possibly made larger (i.e., if the increase does not create a difficulty in swallowing), so that fewer capsules would be required for daily consumption. HG

—Heather S. Oliff, PhD

Editor's note: Blood plasma levels of curcumin are probably not highly important for colon cancer prevention since the curcumin and related compounds act in the intestinal mucosa and are not required to be in systemic circulation. For other types of tumors in other locations such systemic circulation certainly would be necessary. Some recently introduced commercial curcumin formulations are showing enhanced bioavailability. A peer reviewer of this trial review noted that researchers looked only at rectal biopsies—presumably due to their proximal access, raising the question as to whether curcumin may be more active in the upper areas of the colon.

Comprehensive Review of Phase 2® White Bean Intake for Weight Loss and Glycemic Control by Preventing Carbohydrate Absorption

Barrett ML, Udani JK. A proprietary alpha-amylase inhibitor from white bean (*Phaseolus vulgaris*): A review of clinical studies on weight loss and glycemic control. *Nutr J.* 2011 Mar 17;10:24. doi:10.1186/1475-2891-10-24.

Obesity and its associated health risks are a medical problem worldwide. In addition to exercise and control of diet, foods that slow the absorption of carbohydrates can be an effective therapy. White bean (*Phaseolus vulgaris*, Fabaceae) includes alpha-amylase and glucosidase inhibitors, which inhibit the enzymes that break down carbohydrates. The authors review the evidence that a branded, proprietary product can induce weight loss and reduce the spike in blood sugar that occurs with ingestion of carbohydrates.

Carbohydrates that consist of monosaccharides are absorbed quickly in the intestine and are called "high glycemic foods," while those that consist of polysaccharides are absorbed more slowly and are called "low glycemic foods." After eating high glycemic foods such as white bread, potatoes, and dates, there is a rapid spike in blood sugar and insulin levels. This can lead to the accumulation of lipids in the muscles and liver, and begins the progression to insulin insensitivity and type 2 diabetes. Spikes in blood sugar and increased insulin levels can also be key factors in the development of cardiovascular disease (CVD). Therefore, the type of carbohydrate ingested is highly significant. Carbohydrates that are naturally found in seeds, legumes, and unprocessed whole grains are "resistant" to digestion. Adding resistant starches to foods, such as bread, pasta, and nutrition bars, can be an effective way to lower the glycemic index (GI) of the food.

Another way to alleviate the spike in blood sugar and insulin that follows carbohydrate consumption is to prevent the breakdown of the carbohydrate in the intestine. Several pharmaceutical drugs such as Acarbose (Prandase®, Precose®) act in this way and have been shown to reduce the incidence of CVD and hypertension, as well as to improve insulin resistance in type 2 diabetes patients. Certain compounds in plants have shown similar effects; for example, raspberries (*Rubus idaeus* ssp. *Idaeus*, Rosaceae) and strawberries (*Fragaria* spp., Rosaceae) contain anthocyanins that inhibit α-amylase activity and ellagitannins which inhibit α-glucosidase activity.

α-Amylase inhibitors are also present in grains and beans. The most amount of research along these lines has been done on white beans, specifically the branded product Phase 2® Carb Controller (Pharmachem Laboratories; Kearny, New Jersey). It contains three isoforms of the alpha-amylase inhibitor (α-A1, α-A12, and α-AIL), which act by completely blocking access to the active site of the α-amylase enzyme. Early studies at the Mayo Clinic using a purified concentrate (6-8 times the protein content) showed it inactivated alpha-amylase in the saliva and intestine in a dose-dependent manner in humans. In one study using 5 g and 10 g of white bean extract (introduced via intubation), intestinal amylase was inhibited by 95% in 15 minutes, and the receipt of carbohydrates into the distal parts of the small bowel was increased by 22-24% (showing that the carbohydrates had not been absorbed in the upper intestine). The white bean preparation also reduced the spike in blood glucose by 85% and minimized the subsequent dip of blood glucose levels following metabolism. Levels of insulin, C-peptide, and gastric inhibitory polypeptide were also lower. Additional studies conducted with diabetics showed that as little as 2.9 g of whole white bean extract, taken as a powder or tablet, produced statistically significant differences in the same parameters. A longer-term study (3 weeks) with higher doses (4-6 g) also confirmed these benefits. Gastrointestinal symptoms and diarrhea that occurred in some subjects on the first day resolved within a few days of continuing the supplement.

The Phase 2 Carb Controller product is a water extract produced from non-genetically modified organism (non-GMO) whole white beans, which are ground and then extracted for 4 hours. Phase 2 is odorless and tasteless and was designed to be more potent and stable than the earlier product tested by the Mayo Clinic. It can be used in powder, tablet, capsule, or chewable form, and is contained in approximately 200 products worldwide, including chewing gum, mashed potatoes, and yeast-raised dough. Typical dosing for the capsule form is 1 to 2 capsules (500 mg per capsule), taken before each of 3 daily meals, for a total of 1500 to 3000 mg per day.

Phase 2 has been tested in 10 clinical studies that demonstrated weight loss over time. Four studies compared Phase 2 to a placebo using doses ranging from 445 mg for 4 weeks to 3000 mg for 4 to 12 weeks. In a 12-week randomized, double-blind, placebo-controlled study in overweight individuals (n=60; body mass index [BMI] between 24 and 32 kg/m^2) consuming 3000 mg/day of Phase 2 in the form of a soft chew, subjects had an average loss of 6.9 lbs (3.1 kg), while the placebo group gained just under a pound. A randomized, double-blind, placebo-controlled study performed in China (n=101) used 3000 mg of Phase 2 split into 3 doses per day for 60 days, with an average weight loss of 4.9 lbs (1.9 kg) compared to 0.88 lbs (0.4 kg) in the placebo group (P<0.0001).

A third randomized, double-blind, placebo-controlled study in slightly overweight subjects (n=60) utilized a combination tablet of 445 mg Phase 2 and 0.5 mg of chromium picolinate per day taken before a high-carbohydrate meal. After 30 days, subjects had an average weight loss of 6.45 lbs (2.93 kg) compared with 0.77 lbs (0.35 kg) in the placebo group (P<0.001). There were also significant differences in BMI, fat mass, adipose tissue thickness, and waist/hip/thigh circumferences while maintaining lean body mass. A fourth study in overweight adults used 2000 mg of Phase 2 split into 2 doses per day for 4 weeks in addition to nutritional guidance, an exercise program, and psychological counseling. In this study, both the treatment and placebo groups lost weight (6.0 lbs [2.7 kg] and 4.7 lbs [2.1 kg], respectively), and there was no statistically significant difference between them. When stratified by carbohydrate intake, they demonstrated that the more carbohydrate ingested, the greater the weight loss. No adverse effects were reported in any of the 4 trials.

Three studies demonstrated the efficacy of Phase 2 for weight loss over time, but did not provide significant comparisons to a placebo group. A randomized, double-blind, placebo-controlled trial (n=40) in overweight adults utilized a proprietary blend (Suco-Bloc®; Med-Eq AS; Norway) containing 200 mg of Phase 2 (Phaseolamin®; Leuven Bioproducts; Belgium), 200 mg of inulin (from chicory [*Cichorium intybus,* Asteraceae] root), and 50 mg of garcinia (*Garcinia cambogia*, Clusiaceae) extract. There was a significant reduction in weight for the treatment group of 7.7 lbs (3.5 kg; P=0.001), while the placebo group lost 2.9 lbs (1.3 kg); body mass analysis showed this was mostly due to loss of fat.

In the second study, which was double-blind and placebo-controlled (n=60), subjects took 2 capsules of Thera-Slim™ (ProThera; Reno, Nevada) containing 500 mg Phase 2 plus 250 mg fennel (*Foeniculum vulgare*, Apiaceae) seed powder, or placebo, for 12 weeks along with meals containing 100-200 g of carbohydrates. After the first 12 weeks, the treatment group lost 1.4 lbs (0.64 kg), while the placebo group gained an average of 0.6 lbs (0.27 kg). Also after the initial 12 weeks, all subjects took the Phase 2 product for an additional 12 weeks. Lastly, a randomized, double-blind, placebo-controlled study in obese subjects (n=39) taking 3000 mg of Phase 2 per day for 8 weeks following carbohydrate meals averaged a weight loss of 3.79 lbs (1.7 kg) compared with the placebo group, which lost an average of 1.65 lbs (0.75 kg); the between-group difference was not statistically significant. No adverse effects were noted in any of these 3 studies.

Several open-label studies on weight loss have also been conducted. One study was conducted with Phaseolamin™ 1600 diet (Metabolic Company, Ltd; Japan; 750 mg Phase 2, 200 mg clove [*Syzygium aromaticum*, Myrtaceae], 20 mg lysine, 20 mg arginine, and 20 mg alanine) in overweight subjects (n=10). After 8 weeks, the subjects' body weight decreased significantly (2.4%; 74.5±7.3 kg to 72.7±7.8 kg; P=0.002), as did caloric intake (P=0.01), body fat (P<0.001), BMI (P=0.002), and blood lipids. A second study (n=37) used Precarb (Carb Intercept; Natrol; Chatsworth, California) at a dose of 2 capsules, 3 times daily with high-carbohydrate meals for 30 days. Body weight decreased by 5.15 lbs (2.34 kg; P<0.001), and there was also a significant reduction in mean waist-to-hip ratio of 2.77±2.55 (P<0.001). Another study used Super Bows Diet Type B (Japan), which contains 500 mg Phase 2, forskohlii (*Plectranthus barbatus*, Lamiaceae, syn. *Coleus forskohlii*) extract, and mushroom chitosan (Plus fort Barrious®; Barrious Laboratories; Tokyo, Japan), and was taken as a powder in water before lunch and dinner. There was no change in caloric intake, but total cholesterol did decrease significantly (P<0.05). Minor gastrointestinal symptoms with this product resolved after a few days of use.

Four crossover studies assessed the effect of Phase 2 on glycemic control and showed that the product could reduce spikes in blood sugar after a meal in a dose-dependent manner. A placebo-controlled, crossover study tested the blood sugar after consumption of 4 slices of bread with margarine in 11 subjects. In comparison to controls, glucose levels returned to normal 20 minutes sooner when subjects took 1500 mg of Phase 2. The area under the plasma glucose vs. time curve (AUC) was 66% smaller compared to the control (P<0.05). In the same study, 7 subjects were given a full meal (630 calories with 64 g carbohydrates) with or without 750 mg of Phase 2. The average plasma glucose vs. time curve was reduced by 28% with the Phase 2. The authors conclude that there is a dose-related effect, with 1500 mg of Phase 2 being twice as effective as 750 mg. A 6-arm crossover study comparing a capsule and powder form of Phase 2 in 3 doses of 1500, 2000, and 3000 mg showed that only the 3000 mg powder dose caused significant reductions in the GI following a carbohydrate load. A study using Super Bows Diet Type B (n=13) showed that both blood sugar and plasma insulin levels decreased 30 minutes after consumption of carbohydrates (both P<0.01).

With respect to safety, there were no reports of serious adverse side effects in human studies with doses up to 3000 mg of Phase 2 for 24 weeks. There were no reported adverse reactions or signs of toxicity in an acute animal toxicity study (doses of 500-5000 mg/kg) or a 90-day subchronic study (doses of 200-1000 mg/kg). The no-observed-adverse-effect level (NOAEL) was established to be 2500 mg/kg/day, and an independent safety review by Cantox Health Sciences International concluded that it is safe for humans to consume up to 10 g of Phase 2. While raw beans contain phytohaemagglutinin, which can cause severe gastrointestinal disturbances in humans, this compound is found in low levels in white beans and is inactivated by processing.

The authors note that it is difficult to equate different carbohydrate blockers with one another, and therefore they focused on the Phase 2 product only. They conclude that the evidence presented in this paper indicates that Phase 2 reduces the rate of absorption of carbohydrates (thereby reducing the GI of foods) and also promotes weight loss when taken concurrently with meals containing carbohydrates. HG

—Risa Schulman, PhD

Efficacy and Tolerability of Ginkgo Extract in Treatment of Alzheimer's Disease and Vascular Dementia

Reviewed: Ihl R, Tribanek M, Bachinskaya N; for the GOTADAY Study Group. Efficacy and tolerability of a once daily formulation of *Ginkgo biloba* extract EGb 761® in Alzheimer's disease and vascular dementia: Results from a randomised controlled trial. *Pharmacopsychiatry.* 2012;45(2):41-46.

Many studies have demonstrated the safety and efficacy of 240 mg (120 mg 2x/day) of ginkgo (*Ginkgo biloba,* Ginkgoaceae) special extract EGb 761® (Dr. Willmar Schwabe GmbH and Co. KG Pharmaceuticals; Karlsruhe, Germany). Patient compliance is better when patients are required to take fewer daily doses. Therefore, the manufacturer developed a once-daily 240 mg dose of EGb 761. The once-daily dose was tested and found to be safe and efficacious in a previous trial.[1] The goal of the present study was to learn more about efficacy in different types of dementia. This was accomplished by conducting a subgroup analysis of the total population of a randomized, controlled, double-blind, multicenter study.

Since the methods have been described previously, they were mentioned only briefly in this report. Patients were recruited from the outpatient clinic of the Department of Psychiatry of the National Medical University in Kiev, Ukraine, and 19 outpatient clinics of neurological or psychiatric hospitals in Ukraine between April and November 2006. The study included outpatients (n=410, aged ≥ [equal to or greater than] 50 years) with mild to moderate dementia due to probable Alzheimer's disease (AD), possible AD with cerebrovascular disease (CVD), or vascular dementia (VaD).

Clinical diagnosis of AD was established via the criteria of the National Institute of Neurological and Communicative Disorders and Stroke together with the Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA); VaD was established according to the diagnostic criteria published by the National Institute of Neurological Disorders and Stroke together with the Association Internationale pour la Recherche et l'Enseignement en Neurosciences (NINDS/AIREN); and possible AD with CVD was established according to the relevant subsets of those criteria. A recent (≤ [equal to or less than] 1 year old) CT or MRI scan had to be consistent with the clinical diagnosis.

Ginkgo *Ginkgo biloba*. Photo ©2012 Steven Foster

Other inclusion criteria included a score of ≤ 35 on the Test for the Early Detection of Dementia with Differentiation from Depression (TE4D), a total score of 9-23 on the SKT (Erzigkeit's short syndrome test) cognitive test battery, a total score of ≥ 5 on the 12-item Neuropsychiatric Inventory (NPI), and at least one item score (other than delusion or hallucination) of ≥ 3 on the NPI. Patients were excluded if they had significant psychiatric disorders (*e.g.*, major depression or subsyndromal depression), severe somatic disorders, or were taking a medication that could have influenced the assessment scores. Patients were treated with 240 mg EGb 761 or placebo 1x/day for 24 weeks. The primary outcome measures were the SKT and NPI.

A total of 404 patients were included in the analysis, with 333 patients diagnosed as having AD (probable AD: n=121 and possible AD with CVD: n=212) and 71 patients diagnosed as having VaD. Treatment adherence was 99%. For the SKT total score, both subgroups taking EGb 761 had an improvement from baseline by 1.4 points, which was significantly better than the placebo-treated group (AD, P<0.001 and VaD, P<0.05). For the NPI score, VaD patients treated with EGb 761 responded better to treatment than the patients with AD treated with EGb 761 (4.5 point improvement vs 2.9 points, respectively) (P-value not reported). Also for the NPI score, EGb 761-treated patients with AD and VaD improved significantly more than placebo-treated patients (AD, P=0.001 and VaD, P<0.05). When looking at clinically meaningful improvements (decrease in SKT scores by ≥ 3 points or decrease in NPI by ≥ 4 points), 33% of EGb 761-treated patients with AD compared with 14% of placebo-treated patients with AD had clinical improvement on the SKT (P<0.001), and 43% of EGb 761-treated patients with AD compared with 22% of placebo-treated patients with AD had clinical improvement on the NPI (P<0.001). The number of patients with VaD showing clinical improvement was similar to that in patients with AD, but, due to the small size of the VaD subsample, the ginkgo-placebo difference was not statistically significant (for SKT, EGb 761-treated: 28% vs. placebo-treated: 19%, and for NPI, EGb 761-treated: 54% vs. placebo-treated: 31%).

For all secondary outcome variables (NPI caregiver distress score, the Clinical Global Impression of Change as adapted by the Alzheimer's Disease Cooperative Study [ADCS-CGIC], the Alzheimer's Disease Activities of Daily Living International Scale [ADL-IS], and the Verbal Fluency Test), except the dementia quality-of-life scale, there were statistically significant differences between the EGb 761 group and the placebo group in AD as well as in VaD. Quality of life was significantly improved only in AD.

The AD subgroup was further broken down into probable AD and possible AD with CVD. The authors state, "There were no conspicuous differences in efficacy related to vascular pathology."

According to the authors, the most frequently reported adverse events (AEs) were reported with similar frequency among treatment groups, and there were no major bleeding events (data were not provided).

The authors believe that the study population represents everyday practice. The authors conclude that EGb 761 had "essentially similar" effects in patients with AD and VaD. They also think that the data support the use of EGb 761 for dementia as diagnosed in the primary care setting since EGb 761 had similar efficacy for both populations. The study was sponsored by the manufacturer of EGb 761. HG

—Heather S. Oliff, PhD

Reference

1. Ihl R, Bachinskaya N, Korczyn A, et al. Efficacy and safety of a once-daily formulation of *Ginkgo biloba* extract EGb 761® in dementia with neuropsychiatric features: A randomized controlled trial. *Int J Geriatr Psychiatry.* 2011; 26(11):1186-1194.

Ginkgo Extract Improves Complex Memory Function in Healthy, Middle-Aged Subjects

Reviewed: Kaschel R. Specific memory effects of *Ginkgo biloba* extract EGb 761 in middle-aged healthy volunteers. *Phytomed*. November 15, 2011;18(14):1202-1207.

Extracts of ginkgo (*Ginkgo biloba*, Ginkgoaceae) leaves are used to enhance mental performance in people with age-related cognitive impairment. Randomized controlled trials have demonstrated effectiveness of ginkgo extracts in reducing cognitive symptoms in people with dementia. Fewer trials have studied ginkgo in healthy people, and the effects of ginkgo on cognitive function in younger people is not clear, although a previous review of the use of ginkgo extract in controlled clinical trials on healthy subjects indicated that a majority of the trials (13 of 16) resulted in positive outcomes for various cognitive effects, including short-term memory, speed of processing information, etc.[1]

The purpose of this randomized, double-blind, placebo-controlled trial was to investigate the effects of the ginkgo extract EGb 761® (Dr. Willmar Schwabe Pharmaceuticals; Karlsruhe, Germany) on memory in healthy, middle-aged volunteers. The trial was conducted at a single site in Germany by researchers from the University of Osnabrück; Osnabrück, Germany. Subjects were eligible for the trial if they were mentally healthy, well-educated, and 45-65 years of age. Those with cognitive impairment or a history of major depression, anxiety disorder, or substance abuse and those with impaired liver or kidney function or uncontrolled cardiovascular disease or diabetes were excluded from the trial. Eligible subjects were randomly assigned (1:1) to receive either standardized ginkgo extract (EGb 761) or a matching placebo once daily for 6 weeks. Those in the ginkgo group received 240 mg EGb 761, which contained 22-27% ginkgo flavonoids and 5.0-7.0% terpene lactones consisting of 2.8-3.4% ginkgolides A, B, C, and 2.6-3.2% bilobalide, with a content of ginkgolic acids below 5 ppm.

Four assessments were performed at baseline and after 6 weeks of treatment. Two were objective tests of memory. The first objective test measured recall of a detailed list of appointments, including immediate and delayed recall with both qualitative and quantitative components. The second objective test measured recognition of a driving route after watching a film. The third test was a subjective, self-rated memory questionnaire, and the fourth assessment was a questionnaire evaluating well-being and mood. A total of 188 subjects were randomized, and data from 177 subjects were included in the full analysis set. The average age was 54.2 years in the ginkgo group and 54.8 years in the placebo group. The percentage of females was significantly lower in the ginkgo group than in the placebo group (59.1% versus 76.4%, P=0.014), but no gender differences are detected in these tests.

In the demanding appointment recall test, the ginkgo group had greater quantitative improvement than the placebo group from baseline to 6 weeks (P=0.038 for immediate recall and P=0.008 for delayed recall). The ginkgo group had greater qualitative improvement than the placebo group for delayed recall (P=0.010), but not for immediate recall. (The qualitative measure is the ratio of errors to correct answers.) In the less demanding driving route recognition test, changes were similar in both groups from baseline to 6 weeks. Both groups had small, similar improvements on the subjective memory questionnaire, yet there was a trend in favor of ginkgo extract in the factor score including prospective everyday memory (P=0.58), which ties in well with the results of the appointments test. There were no changes in well-being and mood ratings for either group over the 6-week period. The number of adverse events was similar in both groups and no serious adverse events were reported. Causation could not be ruled out for gastric complaints in 3 subjects from each group, headaches in 4 subjects from the ginkgo group, and conjunctivitis and rash in individuals in the placebo group.

The author points out that subjects in this trial were younger and healthier than subjects in many previous studies showing a benefit of ginkgo extract on cognitive performance. Similar outcomes for healthy, elderly subjects have been shown in several studies, though it is generally difficult to detect significant changes in functions of those who are cognitively intact, especially if using measures intended to detect change in the cognitively impaired. The author states the results of this trial "cast doubt on the [previously held] notion that in individuals younger than 60 years effects of ginkgo are lacking."[2]

In this trial, EGb 761 improved memory recall in healthy, middle-aged people performing a complex appointment task. This improvement was not mediated by improvements in mood or in subjective ratings of memory. On the other hand, EGb 761 did not improve performance on a simple test of recognition. According to the author, these results support previous research suggesting that ginkgo extract has very specific patterns of cognitive activity. HG

—Heather S. Oliff, PhD

References

1. Crews WD, Harrison DW, Griffin ML, Falwell KD, Crist T, et al. The neuropsychological efficacy of ginkgo preparations in healthy and cognitively intact adults: a comprehensive review. *HerbalGram.* 2005;67:43-62.
2. Canter PH, Ernst E. *Ginkgo biloba* is not a smart drug: an updated systematic review of randomised clinical trials testing the nootropic effects of *G. biloba* extracts in healthy people. *Hum Psychopharmacol.* 2007;22(5):265-278.

Ginkgo *Ginkgo biloba*. Photo ©2012 Steven Foster

Chocolate Lowers Risk of Coronary Heart Disease: Review and Comments on the National Heart, Lung, and Blood Institute Family Heart Study

Reviewed: Kaynak HE, Taegtmeyer H. Is bitter better? The benefits of chocolate for the cardiovascular system. *Curr Hypertens Rep*. 2011 Dec;13(6):401-403.

Cocoa (*Theobroma cacao*, Sterculiaceae) has shown blood pressure-lowering effects, but its effects on the risk of coronary heart disease (CHD) have not been investigated thoroughly. This article is a report on the cross-sectional National Heart, Lung, and Blood Institute (NHLBI) Family Heart Study,[1] with comments by the authors at the Department of Internal Medicine, Division of Cardiology, University of Texas Medical School at Houston.

In the study, intake of chocolate by 4,970 participants who were 25 to 93 years of age was assessed by using a semi-quantitative food frequency questionnaire. For subjects consuming chocolate 1-3 times per month, 1-4 times per week, or 5+ times per week, the odds ratios (OR) for CHD were 1.01 (95% confidence interval [CI], 0.76-1.37), 0.74 (95% CI, 0.56-0.98), and 0.43 (95% CI, 0.28-0.67), respectively (P for trend < 0.0001), adjusting for age, sex, family, CHD risk group, and a large number of other confounders. This shows a trend of reduced CHD incidence proportional to the increased consumption of chocolate. An additional finding was that subjects who consumed non-chocolate candy 5+ times per week had a 49% higher prevalence of CHD than those who did not (OR, 1.49; 95% CI, 0.96-2.32). The authors of the study concluded that consumption of chocolate is inversely related to CHD in the US.

Based on the above report, the authors Kaynak *et al*. offer the following comments:

> "Cocoa contains a large number of flavanols, which have been shown to positively impact cardiovascular risk factors such as atherosclerosis, platelet function, and endothelial function and regeneration. A notable epidemiological study showed that Kuna Indians who live on an offshore island close to Panama City, Panama and drink water boiled with cocoa beans as their main beverage have a much lower incidence of hypertension even into old age."[2]

By contrast, Kuna people who have moved to the mainland and who drink other beverages (including those that contain store-bought cocoa, largely devoid of flavanols) lose this benefit. In addition, a meta-analysis concluded that cocoa consumption can lower systolic blood pressure by 4.5 mm Hg and diastolic blood pressure by 2.5 mm Hg.[3] Another meta-analysis with similar findings in hypertensive patients indicated a reduction of this magnitude can reduce the risk of a cardiovascular event by more than 20% over 5 years and is comparable to the effect of lifestyle modifications.[4] The effect may be due to increasing the levels of nitric oxide (NO) in the blood and/or inhibition of angiotensin-converting enzyme (ACE).

Chocolate consumption has also been associated with reduction of cardiovascular disease (37%), diabetes (up to 31%), and stroke (29%). A German prospective study showed that in a healthy population, those consuming the least amount of chocolate had the highest incidence of myocardial infarction and stroke, with the inverse being true for those with the highest consumption of chocolate. Similar results were found in elderly Dutch men and postmenopausal American women.

Though many of the findings in this review are positive, the authors note that factors such as local dietary habits and genetic and ethnic disparity should be taken into account when interpreting the studies. They note that it is difficult to have a proper control for double-blind studies, since the bitterness of the flavanols gives away the treatment. Lastly, they purport that the doses of chocolate used in the studies, such as 75 g or 100 g dark chocolate daily to inhibit ACE or lower blood pressure, respectively, are too high for normal daily consumption. Therefore, they conclude that interpretation of studies and meta-analyses should be done prudently. In addition, it must be kept in mind that excessive chocolate consumption may have adverse effects on weight and blood lipid levels, due to the associated calorie intake.

Editor's note: The potential adverse effect of excessive chocolate in food form containing relatively high levels of fat and sugar can be obviated by production of high-flavanol cocoa-derived extracts in dietary supplement form.

—Risa Schulman, PhD

Chocolate *Theobroma cacao*. Photo ©2012 Steven Foster

References

1. Djoussé L, Hopkins PN, North KE, Pankow JS, Arnett DK, Ellison RC. Chocolate consumption is inversely associated with prevalent coronary heart disease: The National Heart, Lung, and Blood Institute Family Heart Study. *Clin Nutr*. 2011;30(2):182-187.
2. McCullough ML, Chevaux K, Jackson L, Preston M, Martinez G, Schmitz HH, Coletti C, Campos H, Hollenberg NK. Hypertension, the Kuna, and the epidemiology of flavanols. *J Cardiovasc Pharmacol* 2006, 47 Suppl 2:S103-S109.
3. Desch S, Schmidt J, Kobler D, et al. Effect of cocoa products on blood pressure: systematic review and meta-analysis. *Am J Hypertens*. 2010;23(1):97-103.
4. Ried K, Sullivan T, Fakler P, et al. Does chocolate reduce blood pressure? A meta-analysis. *BMC Med*. 2010;8:39.

EMI vs. EMA: "Economically Motivated Integrity" vs. Economically Motivated Adulteration in the Natural Products Supply Chain

by Greg Cumberford, President, Bent Creek Institute, Inc.

Editor's Note: As with other guest editorials, Mr. Cumberford's views do not necessarily reflect the views of HerbalGram *or the American Botanical Council.*

An intricate, global network of supply chains produces the botanical and other functional ingredients that are formulated into dietary supplements and functional foods on which Americans rely for daily wellness maintenance. Perhaps in no other major industry in the United States does the term "globalization" better apply. However, an article in the March 2012 issue of *Functional Ingredients* magazine exposed a gap between the American consumer's perception of supplement ingredient origins and the reality.[1] Citing a recent May 2011 survey by United Natural Products Alliance (UNPA), a trade association of dietary supplement producers, *Functional Ingredients* reports that Americans perceive the origins of their supplement ingredients as follows: 77% from the United States, 10% from China, 7% from Europe, and 6% from Japan.

We Americans believe that a large majority of our ingredients comes from domestic US sources and, presumably for botanicals, also from within a USDA Certified Organic inspection and audit framework for cultivated herbs. However, the reality is far different. According to *Functional Ingredients* and UNPA, 60% of the ingredients used in dietary supplements in the United States actually come from China, with 13% from Europe, just 12% from the United States, 10% from Japan, and 5% from other areas. This means that the majority of what we Americans believe comes from domestic sources in fact comes from Asia.

Authenticated botanical voucher specimen for Black Cohosh (*Actaea racemosa* syn. *Cimicifuga racemosa,* Ranunculaceae) archived at Bent Creek Germplasm Repository

To knowledgeable stakeholders in the natural products industry supply chain, the dominance of foreign sourcing for supplement ingredients is an accepted fact. To the consumers and many alternative and integrative healthcare practitioners who accept or even recommend the use of dietary supplements as part of their clinical practice, however, the true origins of their supplement ingredients may be a bit of a revelation.

From traditional botanical ingredients, to marine sources of the popular omega-three fatty acids DHA (docosahexaenoic acid) and EPA (eicosapentaenoic acid), to minerals, vitamins, oils, carotenoids, enzymes, probiotics, and prebiotics, almost every nation and region on Earth supplies the functional ingredients from which finished dietary supplements sold in America are made. Yet in the past decade, global climate change has induced greater turbulence in global weather systems. Political instability, natural disasters, anthropogenic pollution, and other catastrophes have caused greater supply chain disruptions. All the while, cost-conscious consumers are demanding lower prices and greater value in their supplements—thus raising the economic incentive for supply chain players to cut corners on purity, strength, and/or identity in their ingredients, an occurrence known as "economically motivated adulteration," or EMA. Although some ingredient adulteration is surely accidental, based on inadequate quality control procedures or legitimate confusion stemming from differing cultural interpretations of an ingredient's nomenclature, too much of it is intended. Too much of it is designed to evade a responsible distributor's or manufacturer's quality control test methods. Too much is flying under the radar.

Illustrating the complexity and seriousness of EMA, Edward Fletcher of Strategic Sourcing, Inc., and other knowledgeable botanical industry sources claim that globally rising demand and higher supply chain prices for black cohosh root (*Actaea racemosa,* syn. *Cimicifuga racemosa,* Ranunculaceae)—a native forest understory medicinal herb of eastern North America—have revealed significant amounts of circulating raw material to be EMA-tainted material. Much of the adulterated material is derived from various Asian species of *Actaea* including *A. cimicifuga* (formerly *Cimicifuga foetida*, so-called "Chinese" black cohosh—a name that is not accepted by the *American Herbal Products Association's Herbs of Commerce, 2d, ed.*,[2] an FDA-recognized listing of common names for herbs and their corresponding Latin binomials), *A. dahurica,* and *A. heracleifolia*. Other closely related North American species have been identified as adulterants including *A. podocarpa*, *A. pachypoda*, and *A. rubra*, in addition to other native North American forest understory "cousins" to true black cohosh, such as herbs in the genera *Caulophyllum*, *Astilbe* and *Aruncus*—whose above-ground foliage or dried roots can appear visually similar to *A. racemosa* but in fact contain different phyto-complex constituents. Fletcher noted that industry-wide attention to the issue of black cohosh adulteration in recent years has improved overall quality in this herb's supply chain (e-mail, E. Fletcher to G. Cumberford, April 3, 2012).

Joe-Ann McCoy, PhD, Director, Bent Creek Germplasm Repository at The North Carolina Arboretum; Member, ABC Advisory Board

The US Food and Drug Administration (FDA) has mandated in dietary supplement Good Manufacturing Practices (GMPs, 21 CFR 111) that manufacturers conduct 100% identity confirmation tests. Yet the tests deployed must be capable of detecting the known EMAs. Too often this is not happening. If a high degree of material purported to be true black cohosh is in fact EMA-tainted, then all responsible, "ethical supply chain stakeholders must push back with EMI—economically motivated integrity."

EMI means aligning in opposition to EMA through a coordinated approach among foreign and domestic raw material suppliers, consolidators and brokers, US distributors, manufacturers, analytical laboratories, retailers, and trade associations. It means taking a moral, ethical, and scientifically valid stance against EMA on a case-by-case basis. This would be something like a self-policing "neighborhood watch" program along every link of the ingredient supply chain, from raw producer to branded finished product retailer. All supply chain parties have a clear economic incentive to root out EMA. FDA GMPs provide manufacturers with a strong motive not to be linked to an EMA, as a buyer's quickest corrective and preventive action to a discovered adulterant is not to do business with that supplier ever again.

Recently, an industry-funded consortium led by Mark Blumenthal of the American Botanical Council (ABC), Roy Upton of the American Herbal Pharmacopoeia (AHP), and Ikhlas Khan, PhD, of the University of Mississippi's National Center for Natural Products Research (NCNPR)—the ABC-AHP-NCNPR Botanical Adulterants Program—formed to systematically identify botanical EMAs and their detection methods through a series of white papers that will educate industry stakeholders, practitioners, and consumers. Bent Creek Institute, the executive and administrative manager of the new nonprofit US Botanical Safety Laboratory, has committed to supporting this consortium's efforts, as well as the efforts of the American Herbal Products Association's (AHPA) planned Botanical Authentication Wiki Project—a Wikipedia-like resource of herb-specific analytical methods for assuring correct botanical identity. Bent Creek will provide participating analytical laboratories with authenticated botanical reference materials from the Bent Creek Germplasm Repository (under direction of Joe-Ann McCoy, PhD); input on botanical identity confirmation methods backed by authenticated, reproducible, and traceable vouchers; phytochemical and genomic data on adulterants; and will assist supply chain stakeholders in their efforts to produce positive confirmation of the identity, purity, and composition of their herbal ingredients.

In the battle of EMI vs. EMA, EMI will ultimately prevail in the United States when enough of the supply chain players who provide our ingredients align with values-conscious consumers, choosing to reward rigorous science, transparency, and traceability over short-term gain, denial, and deceit. As more branded natural products and supplement companies adopt ingredient and lot traceability platforms, consumers will feel ever more inspired and empowered to choose natural products backed by EMI. HG

Greg Cumberford is the President of Bent Creek Institute, Inc., a nonprofit botanical research, conservation, and strategic services organization based at The North Carolina Arboretum and focused on medicinal plant and endophyte research, analysis, and economic development in Asheville, North Carolina. A veteran of the herbal industry, he was formerly the Vice President of Strategic Initiatives at Gaia Herbs.

References

1. Schultz H. Ingredient insomnia: what keeps supply chain managers up at night? *Functional Ingredients.* March 2012:32.
2. McGuffin M, Kartesz JT, Leung AY, Tucker AO. *American Herbal Products Association's Herbs of Commerce, 2d. ed.*, Silver Spring, MD: American Herbal Products Association., 2000.

MEDICINAL CHINESE TEAS:
A review of their health benefits with a focus on fermented tea

By Tiffany L. Weir, PhD; Yabei Hu, MS; Elizabeth P. Ryan, PhD; Donghe Fu, PhD; Wenjun Xiao, PhD; Wenying Lin, OMD, FABORM, LAc; Paul V. Murray, LAc, FABORM, CNC; Randall Snook, MD

Scientists from Hunan City University prepare experimentally fermented fuzhuan tea for taste-testing. Photo ©2012 Tiffany Weir

Summary

Tea has been enjoyed globally for centuries as a beverage and for its unique medicinal properties. Scientific investigations of the active chemical compounds in tea and their biological mechanisms of action support continued human studies on the prevention and amelioration of chronic diseases. The distinction between different types of teas and their reported health benefits can often be misleading and has been reviewed herein to highlight physical and chemical differences. Because the enzymatic oxidation process is often mistakenly referred to as fermentation, the term "post-fermented" is used to distinguish between teas that have undergone an open-air microbial fermentation step from those teas that have been oxidized only. These post-fermented teas have been ignored largely by Western researchers and are presented as a novel focus area of this review. The emphasis on fuzhuan tea is a result of research conducted in China that suggests that the active components of this tea differ from the catechins and L-theanine that contribute to the bioactivity of green, black, and other kinds of tea. Observational human data suggest that this tea may have unique health properties and that it merits future controlled human clinical trials on the prevention, control, and treatment of cardiovascular disease and Type 2 diabetes.

Introduction

According to Chinese lore, tea was first discovered nearly 5,000 years ago when leaves from a nearby tea tree blew into a cup of warm water belonging to the emperor Shen Nong. From its ancient origins, tea consumption has grown and it is now second only to water in worldwide beverage consumption. It continues to gain popularity in North America because of reported health benefits, including weight loss, chemoprevention, improved immune function, and decreased risk of cardiovascular disease and diabetes.[1-4]

Despite its widespread and rapidly growing popularity, there is considerable confusion regarding what constitutes a tea, differences among types and processing of teas, and their level of oxidation and fermentation. This review is intended to clarify these important distinctions and to introduce fuzhuan tea (also called Golden Flower, Hu Nan Hei Cha, Huajuan, and Hu or Fu Brick tea), a unique type of post-fermented tea from China. Observational results from Asian populations who eat high-fat, meat-based diets, but also consume fuzhuan tea daily, strongly suggest lipid

Tea *Camellia sinensis.* Photo ©2012 Steven Foster

protective/lowering effects of this tea.[5,6] These observations have led to pre-clinical studies in models of hyperlipidemia.[5,6] Human observational studies in the United States are underway to address whether fuzhuan tea can alter blood lipid profiles (*i.e.,* lowering low-density lipoprotein [LDL], raising high-density lipoprotein [HDL], altering particle size). Accumulating scientific evidence suggests that this post-fermented tea may become a viable alternative to statins and other medications. It may have utility as a dietary supplement for individuals with elevated cholesterol who are at high risk for cardiovascular disease and plan to manage disease risk without medication.[7]

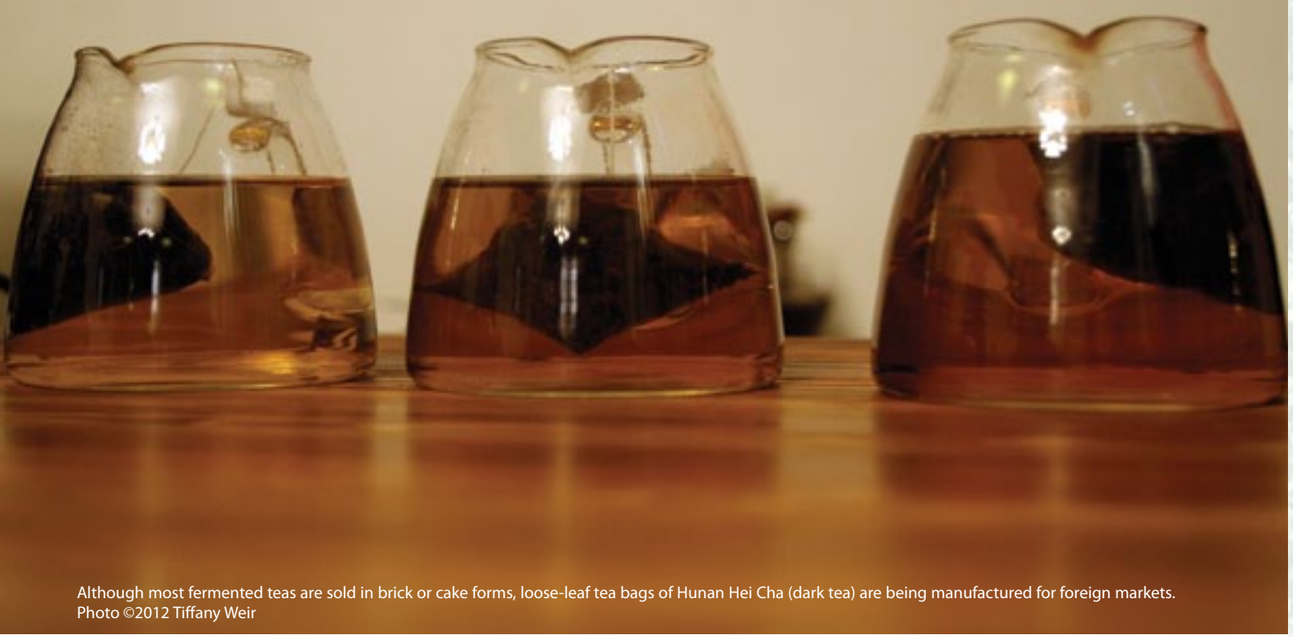
Tea Origins and Processing

Tea is a beverage made from the leaves, buds, stems, and nodes of the plant *Camellia sinensis* (Theaceae), an evergreen shrub originating from Southeast Asia, which is now cultivated in tropical and subtropical regions worldwide. Beverages made of chamomile (*Matricaria recutita*, Asteraceae), echinacea (*Echinacea purpurea*, Asteraceae), yerba mate (*Ilex paraguariensis*, Aquifoliaceae), and other herbs, for example, are frequently referred to as teas, although they contain no *C. sinensis* and are more accurately called infusions or tisanes.[8,9] Although there are several varieties of *C. sinensis*, only two of these make up the majority of commercial tea production. These major varieties are *C. sinensis* var. *sinensis,* which originated in China, has smaller leaves, and grows at higher altitudes; and *C. sinensis* var. *assamica,* a larger-leafed variety from the Assam region of India that is adapted to lower elevation. Other varieties include *C. sinensis* var. *parvifolia*, a lesser known hybrid of *assamica* and *sinensis*; *C. sinensis* var. *cambodiensis,* "the Java bush;" and *C. sinensis* var. *waldenae*, which had been considered a separate species but recently was reclassified as a variety of *C. sinensis*.[10] For the tea drinker, typically the beverage is distinguished more by the steps that go into processing the teas than the variety of plant used (Figure 1). Depending on the age of the leaves, the extent of oxidation, post-harvest treatment, and quality of the final product, currently most teas are classified as white, green, yellow, oolong, black, and dark teas.

The steps of tea processing include wilting, rolling, oxidation, heat fixing (a step to stop the oxidation process), yellowing (only with yellow tea), shaping, drying, and curing. A tea is classified depending on the number and sequence of these steps that it undergoes. Wilting is a process by which newly picked leaves are thinly spread to air dry. In areas where the climate is too moist, heated air is forced through the leaves. This step reduces the water content of the leaves, but they remain pliable enough for rolling. Rolling of the leaves is conducted either by machine or by hand to break the cells, releasing oils that give the tea its distinctive aroma. Rolling can also activate enzymes in the cells resulting in oxidation of the leaves and is not to be confused with the microbial fermentation process exclusive to post-fermentation tea processing. During oxidation, the chlorophyll is broken down, causing the leaves to turn brown and release tannins. The oxidation is stopped by a drying step, which evenly dries the leaf without burning it and inactivates the enzymes that result in oxidation. Green, yellow, oolong, white, and black teas are primarily determined by their level of oxidation, while all dark teas undergo a microbial fermentation step and are usually sold as bricks or cakes. Green, dark, and yellow teas may or may not be wilted, and are then pan-fried or steamed (heat-fixed) to prevent oxidation, resulting in leaves that remain green. Black teas are rolled and fully oxidized, while oolong teas are often shaken rather than rolled and then only partially oxidized before drying. White tea is the least processed form of tea. It is made from buds and young leaves of plants that are picked in early spring and air-dried to prevent oxidation.

Tea Polyphenols and Health Benefits

As a result of the different processing methods, each type of tea has a different chemical content that results in distinctive flavors,



Although most fermented teas are sold in brick or cake forms, loose-leaf tea bags of Hunan Hei Cha (dark tea) are being manufactured for foreign markets.
Photo ©2012 Tiffany Weir

Although the purported benefits of tea polyphenols have been widely touted, the majority of the evidence has been generated from studies in cell lines, animal models, or derived from epidemiological observations, and reports from the existing human clinical trials are conflicting.

colors, and health benefits. In general, the health-promoting properties of green teas are the best-studied and are largely attributed to a class of polyphenolic compounds, including but not limited to the family of catechins comprising the following: epicatechin (EC), epicatechin gallate (ECG), and epigallocatechin gallate (EGCG).[11] Catechins are natural antioxidants that contribute to a number of reported biological activities such as protection against cancer and cardiovascular disease, antimicrobial and antiviral properties, and modulation of obesity and insulin resistance.[12,13] Oolong and black teas, originally valued for their deep, rich flavors, lose many of these beneficial catechin compounds during oxidation.[14,15] During the oxidation process, catechins are converted to other classes of polyphenolic compounds known as theaflavins and thearubigens, which are potent antioxidants and impart different health benefits than the polyphenols from green teas.[15]

Although the purported benefits of tea polyphenols have been widely touted, the majority of the evidence has been generated from studies in cell lines, animal models, or derived from epidemiological observations, and reports from the existing human clinical trials are conflicting. Inconclusive findings regarding therapeutic or protective effects of teas against cancer and Type 2 diabetes have been summarized in recent meta-analyses.[16,17,18,19] Studies indicating efficacy of tea polyphenols for reducing body fat and lowering lipid levels are equally confounding. Although several human intervention studies have shown that orally administered tea polyphenols result in weight loss, lower body mass index (BMI), and reduced LDL,[20,21] other studies showed significant decrease in body weight but without corresponding reduction in body fat or hip:waist ratios.[22,23] There are many confounding factors that must be accounted for, including human genetics, differences in tea preparation, variation in tea bioactive chemicals, and bioavailability/metabolism of these bioactive components. Furthermore, these results highlight the need for controlled human studies conducted in diverse populations and clear identification of and amount of the bioactive chemical linked to the specific biological activity under investigation.

Table 1. Examples of Different Dark Teas and Their Processing Methods.

Tea	Province of Origin	Processing Method	Additional information
Liu Bao	Guangxi, Guangong	pile-fermented, aged in bamboo baskets	Partially oxidized *C. sinensis* var. *assamica*
Qing Zhuan	Hubei	pile-fermented	Leaves from older, selenium-enriched plants from the western part of the province
Mi Zhuan	Hubei	natural aging methods	Made from fully oxidized tea leaves
Fuzhuan	Hunan	pile-fermented followed by *E. cristatum* development	Brick forms contain stems and twigs, visible "golden flower"
Hua Juan/ Qian Liang	Hunan	naturally aged and stored in bamboo or palm mats	Processed by hand
Xiang Jian	Hunan	pile-fermented, aged in bamboo baskets	Harvested during the "Grain rain" season, no step to stop oxidation
Kang Zhuan	Sichuan	pile-fermented	
Pu'erh	Yunnan	naturally aged or pile-fermented	**Connoisseur's tea, *C. sinensis* var. *assamica***

Post-Fermented or Dark Teas

In addition to the well-known and widely consumed teas discussed above, a unique processing method that involves microbial fermentation is used for the production of dark or post-fermented tea. Most post-fermented teas start with a process to stop oxidation, similar to green tea, but are then subjected to a microbial fermentation step that gives the leaves a darker color and alters their flavor. Raw dark teas are steamed and compressed into cakes or bricks (zhuan) and aged over a period of years. These rare and expensive age-fermented teas are highly coveted by tea connoisseurs, although their origins are much more humble. Traditionally, these teas were compressed to facilitate their transport by donkey or horse and preserve them for trade to the northwestern provinces where natural fermentation would occur by common microbes such as *Sacchromyces* spp. (Saccharomycetaceae; brewer's yeast) and *Aspergillus spp.* (Trichocomaceae; bread molds). These teas were historically traded by way of the "Tea Horse Road" and were highly valued for their health properties among nomadic populations who largely consumed high-fat and protein-based diets.[24]

Figure 1. Stages of Tea Processing

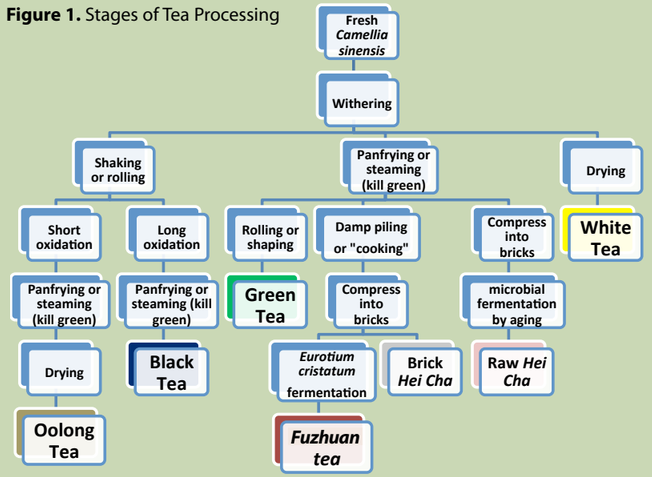


Figure 2. Production of fuzhuan tea. (A) Harvest of *Camellia sinensis* leaves in Hunan province. (B) After oxidation is stopped by steaming, an initial fermentation step occurs by damp piling the tea leaves. (C) Tea leaves are re-steamed and compressed into bricks. (D) Fuzhuan bricks are subjected to an additional fermentation process where its distinguishing feature, the visible yellow fungal colonies (inset) of *Eurotium cristatum* develop.
Photos ©2012 Paul V. Murray and Wenying Lin

Post-fermented brick teas differ from raw dark teas because they undergo a multi-step curing process referred to as "cooking" or "ripening." Cooking consists of piling, dampening, and turning the leaves in a manner similar to compost, resulting in a much faster secondary fermentation while replicating the taste of naturally aged raw-brick teas. Post-fermented teas are not to be confused with kombucha, a fermented beverage of Russian origin. Kombucha is made by adding a symbiotic colony of bacteria and yeast (scoby) to ferment an infusion made with tea leaves or herbs and sweetened with sugar. The scoby usually contains various yeasts and acetic acid-producing bacteria, such as *Gluconacetobacter xylenus* (Acetobacteraceae), which converts the alcohols produced by the yeasts into acetic acid.[25]

Outside of China, Pu'erh tea is the most popular dark tea and its origins, processing, and health benefits have been reviewed recently.[24] Many westerners believe that Pu'erh is synonymous with fermented dark teas, and a significant point of clarification and synthesis for this review is that Pu'erh is only one of several specific types of post-fermented brick tea. Other brick teas include Hei zhuan, Mi zhuan, Kang zhuan, Qing zhuan, Liu bao, Hua zhuan, and Fuzhuan tea. While these post-fermented teas are considered to be similar, they are distinguished by their region of origin and methods of fermentation (Table 1). Fuzhuan tea comes from Hunan Province, China, and undergoes a consistent and regulated modern process of post-fermentation (Figure 2). This post-fermented tea is produced by the damp-piling method, but unlike the other post-fermented teas that widely vary in microflora from factory to factory, fuzhuan tea is also intentionally fermented with a fungus, *Eurotium cristatum* (Trichomaceae),

Fungal growth of *Eurotium cristatum*, the "Golden Flower," is visible as a yellow powder on fuzhuan tea leaves. Photo ©2012 Tiffany Weir

called the "golden flower" (Figure 2D). This fungus, originally isolated and described in association with stored corn in South Africa[26] is the dominant micro-organism present during fermentation of fuzhuan tea.[27] *Eurotium cristatum* is closely related to molds in the genus *Aspergillus,* a group of fungi that has a wide range of industrial uses[28,29] and whose consumption is generally regarded as safe (GRAS) by the US Food and Drug Administration.[30] Fermentation of tea leaves by *E. cristatum* is thought to impart unique chemical properties and bioactivity to fuzhuan tea, and the quality of a brick is often determined by the prevalence of "golden flowers" on its surface.

Interestingly, fermentation by *E. cristatum* has been shown to reduce the amount of catechins, caffeine, and amino acids found in fuzhuan tea, and the levels of theaflavin and thearubigin vary dramatically.[31] Thus, this tea has lower levels of the compounds thought to impart bioactivity than other teas.[32,33] However, a recently published report identified several novel triterpenoid compounds from fuzhuan tea, but their significance as bioactive components of the tea has not yet been determined.[34] In addition, *E. cristatum* produces unique fungal metabolites, such as anthraquinone pigments including emodin and catenarin,[35] which have reported bioactivities. Emodin was recently shown to inhibit 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1), a promising therapeutic target in type 2 diabetes, and also reduced prednisone-induced insulin resistance in a diet-induced diabetic mouse model.[36] Catenarin, the most abundant anthraquinone detected in the mycelia and the culture filtrates of *E. cristatum* has antimicrobial properties.[35,37] The authors' laboratories are currently exploring chemical differences between fuzhuan tea and a variety of green teas and have tentatively identified several fatty acid amides (Keller *et al.*, unpublished data) that are catabolically related to cannabinoids and are thought to promote sleep.[38]

Despite lower levels of the polyphenols believed to impart tea's health-promoting effects, results from several *in vitro* and *in vivo* animal studies indicate that fuzhuan tea and its extracts show activity in reducing hyperlipidemia.[5,6,32] In addition, the tea was shown to be active at inhibiting growth of 2 gastrointestinal cancer cell lines.[39] A recently published study reporting observational data from 10 individuals showed that individuals who consumed the tea for 120 days showed significantly lower total cholesterol, LDL, and HbA1c levels, and higher HDL when compared to historical controls.[7] Although further studies are needed to assess the clinical efficacy of this tea for cancer and cardiovascular benefits, *in vitro* activities and phytochemical characterization suggest that the biological activity of this tea may be due to novel compounds resulting from *E. cristatum* fermentation.

Conclusion

The study of fuzhuan tea has been at the forefront of tea research throughout China, but has not been available for scientific study and consumption in the United States until recently. In addition to compelling data suggesting that this tea can regulate blood sugars and cholesterol,[7] fuzhuan tea has been shown in Chinese studies *in vitro* and in animal and human models to promote weight loss,[5] aid in digestion,[40] prevent certain gastric cancers,[39] and treat secretory diarrhea.[41] Future studies on fuzhuan tea will be focused on identifying novel active chemical components and their cellular targets, and on identifying the tea's ability to modulate native microflora in the gut. A healthy gut flora aids in digestion, prevents pathogen colonization, and modulates mucosal and systemic immune responses and inflammation.[42] Promotion of healthy commensal bacteria by fuzhuan tea could provide a mechanism for the broad range of reported effects of this tea. Ultimately, controlled human clinical studies will also be needed to validate the various ethnobotanical medicinal uses of this tea. HG

Tiffany Weir is an assistant professor of food science and human nutrition at Colorado State University. She can be reached for correspondence at tiffany.weir@colostate.edu.

Dr. Elizabeth Ryan is an assistant professor of toxicology and nutrition in the Department of Clinical Sciences at Colorado State University.

Dr. Wenjun Xiao and Dr. Donghe Fu are professors in the National Research Center of Engineering and Technology for Utilization of Functional Ingredients from Botanicals at Hunan Agricultural University, Changsha, China. Dr. Xiao can be reached for correspondence at xiaowenjun88@sina.com.

Ms. Yabei Hu is an assistant researcher in the National Research Center of Engineering and Technology for Utilization of Functional Ingredients from Botanicals at Hunan Agricultural University.

Randall Snook, MD, is an internist/gerontologist in private practice in Lone Tree, Colorado, a graduate of Colorado State University, and founder of Advanced Integrative Medicine, PC and Teadoc, LLC.

Wenying Lin is a Chinese medical doctor and Paul V. Murray is a Chinese medical practitioner. They are co-owners of Whole Health Centers and Golden Flower Trading Company.

Disclosure: Paul V. Murray and Wenying Lin distribute fuzhuan tea under the trade name PHatea.

References

1. Widlansky ME, Duffy SJ, Hamburg NM, et al. Effects of black tea consumption on plasma catechins and markers of oxidative stress and inflammation in patients with coronary artery disease. *Free Radic Biol Med.* 2005;38(4):499-506.
2. Schneider C, Segre T. Green Tea: Potential Health Benefits. *Am Fam Physician.* 2009;79:591-594.
3. Cooper R, Morre DJ, Morre DM. Medicinal benefits of green tea part I. Review of Non Cancer Health Benefits. *J Altern Complement Med.* 2005;11:521-528.
4. Cooper R, Morre DJ, Morre DM. Medicinal benefits of green tea part II. Review of AntiCancer Properties. *J Altern Complement Med.* 2005;11:639-652.
5. Xiao WJ, Ren GP, Fu DH, Gong ZH, Xiao LZ, Liu ZH. Study on the regulation of blood lipid by fuzhuan tea. *Cha Ye Ke Xue.* 2007;27:211-214.
6. Fu DH, Liu ZH, Huang J, Gong YS, Chen JH. Research of fuzhuan tea's therapy for hyperlipidemia by high-throughput screening. *Cha Ye Ke Xue.* 2006;26:209-214.
7. Fu D, Ryan EP, Huang J, et al. Fermented *Camellia sinensis*, fuzhuan tea, regulates hyperlipidemia and transcription factors involved in lipid catabolism. *Food Res Int.* 2011:in press.
8. Martin LC, Cooper R. From herbs to Medicines: a world history of tea—from legend to healthy obsession. *Alternative and Complementary Therapies.* 2011;17(3):162-168.
9. Martin LC. *Tea, the Drink that Changed the World*. Atlanta: Tuttle Publishing; 2007.
10. Ming TL. A revision of Camellia sect. *Thea. Acta Botanica Yunnanica.* 1992;14:115-132.
11. Lunder TL. Catechins of green tea: antioxidant activity. *Phenolic compounds in food and their effects on health.* American Chemical Society; 1992.
12. Zaveri NT. Green tea and its polyphenolic catechins: medicinal uses in cancer and noncancer applications. *Life Sci.* 2006;78(18):2073-2080.
13. Liao S, Kao Y-H, Hiipakka RA. Green tea: biochemical and biological basis for health benefits. *Vitam Hormon.* Vol Volume 62: Academic Press; 2001:1-94.
14. Lin Y-S, Tsai Y-J, Tsay J-S, Lin J-K. Factors affecting the levels of tea polyphenols and caffeine in tea leaves. *J Agric Food Chem.* 2003;51(7):1864-1873.
15. Leung LK, Su Y, Chen R, Zhang Z, Huang Y, Chen Z-Y. Theaflavins in black tea and catechins in green tea are equally effective antioxidants. *J Nutr.* September 1, 2001 2001;131(9):2248-2251.
16. Iwasaki M, Inoue M, Sasazuki S, et al. Green tea drinking and subsequent risk of breast cancer in a population to based cohort of Japanese women. *Breast Cancer Res.* 2010;12(5):R88.
17. Ogunleye A, Xue F, Michels K. Green tea consumption and breast cancer risk or recurrence: a meta-analysis. *Breast Cancer Res Treat.* 2010;119(2):477-484.
18. Jing Y, Han G, Hu Y, Bi Y, Li L, Zhu D. Tea consumption and risk of type 2 diabetes: a meta-analysis of cohort studies. *J Gen Intern Med.* 2009;24(5):557-562.
19. Kakuta Y, Nakaya N, Nagase S, et al. Case–control study of green tea consumption and the risk of endometrial endometrioid adenocarcinoma. *Cancer Causes Control.* 2009;20(5):617-624.
20. Nagao T, Hase T, Tokimitsu I. A green tea extract high in catechins reduces body fat and cardiovascular risks in humans. *Obesity.* 2007;15(6):1473-1483.
21. Nagao T, Komine Y, Soga S, et al. Ingestion of a tea rich in catechins leads to a reduction in body fat and malondialdehyde-modified LDL in men. *Am J Clin Nutr.* January 1, 2005 2005;81(1):122-129.
22. Diepvens K, Kovacs EMR, Nijs IMT, Vogels N, Westerterp-Plantenga MS. Effect of green tea on resting energy expenditure and substrate oxidation during weight loss in overweight females. *Br J of Nutr.* 2005;94(06):1026-1034.
23. Auvichayapat P, Prapochanung M, Tunkamnerdthai O, et al. Effectiveness of green tea on weight reduction in obese Thais: A randomized, controlled trial. *Physiol Behav.* 2008;93(3):486-491.
24. Ahmed S, Freeman M. Pu'erh tea and the Southwest Silk Road: an ancient quest for well-being. *HerbalGram.* 2011;90:32-43.
25. Nguyen V, Flanagan B, Gidley M, Dykes G. Characterization of cellulose production by a Gluconacetobacter xylinus strain from kombucha. *Curr Microbiol.* 2008;57(5):449-453.
26. Raper, Fennell. *The Genus Aspergillus* 1965.
27. Liu ZY, Xu AQ, Li ZJ, Wang YL. Research progress on *Eurotium cristatum* and its metabolites in fuzhuan tea. *Tea Communication.* 2010;37:23-26.
28. Powell KA. *The genus aspergillus from taxonomy and genetics to industrial application*. New York: Plenum; 1994.
29. Wood BJB. Oriental food uses of Aspergillus. In: Smith JE, Pateman JA, eds. *Genetics and Physiology of Aspergillus*. London: Academic Press; 1977:481-498.
30. US-FDA/CFSAN. Gras Notice Inventory. 11/9/2009; http://www.fda.gov/Food/FoodIngredientsPackaging/GenerallyRecognizedasSafeGRAS/GRASListings/default.htm. Accessed July 20,2011.
31. Huang Q, Li YP, Chen LJ, Chen K. Study of chages in active components in dark tea (fuzhuan tea) during liquid fermentation by Eurotium cristatum. *Journal of Tea Science.* 2007;28(231-234).
32. Fu DH, Liu ZH, Huang JA, Hao F, Wang F, Lei YG. Variations of components of fuzhuan tea during processing. *Cha Ye Ke Xue.* 2008;29:64-67.
33. Zhu QI, Clifford MN, Mao QL, Deng FM. Comparative study on the components of Pu'er tea and Fu-brick tea with black tea by LC-MS. *Journal of Tea Science.* 2006;26:191-194.
34. Ling T-J, Wan X-C, Ling W-W, et al. New triterpenoids and other constituents from a special microbial-fermented tea—fuzhuan brick tea. *J Agric Food Chem.* 2010;58(8):4945-4950.
35. Anke H, Kolthoum I, Zähner H, Laatsch H. Metabolic products of microorganisms. 185. The anthraquinones of the *Aspergillus glaucus* group. I. Occurrence, isolation, identification and antimicrobial activity. *Arch Microbiol.* 1980;126(3):223-230.
36. Feng Y, Huang S-l, Dou W, et al. Emodin, a natural product, selectively inhibits 11β-hydroxysteroid dehydrogenase type 1 and ameliorates metabolic disorder in diet-induced obese mice. *Br J Pharmacol.* 2010;161(1):113-126.
37. Wakuliński W, Kachlicki P, Sobiczewski P, et al. Catenarin production by isolates of Pyrenophora tritici-repentis (Died.) Drechsler and its antimicrobial activity. *J Phytopathol.* 2003;151(2):74-79.
38. Huang J-K, Jan C-R. Linoleamide, a brain lipid that induces sleep, increases cytosolic Ca2+ levels in MDCK renal tubular cells. *Life Sciences.* 2001;68(9):997-1004.
39. Song LB, Huang JA, Liu ZH, Huang H, Wang KB. Study of the activity of dark (fuzhuan) tea to gastrointestinal tumor. *Cha Ye Ke Xue.* 2009;29:191-195.
40. Wu YY, Ding L, Xia HL, Tu YY. Analysis of the major chemical compositions in fuzhuan brick-tea and its effect on activities of pancreatic enzymes in vitro. *Afr J Biotechnol.* 2010;9:6748-6754.
41. Yu Z-y. Research of the Anti-Diarrhea Function of Fuzhuan Tea.*Cha Ye Ke Xue.* 2009;29:465-469.
42. van Hylckama Vlieg JET, Veiga P, Zhang C, Derrien M, Zhao L. Impact of microbial transformation of food on health--from fermented foods to fermentation in the gastro-intestinal tract. *Curr Opin Biotechnol.* 2011;In Press, Corrected Proof.

Sausage Tree *Kigelia pinnata*. Photo ©2012 PhytoTrade Africa

Sausage Tree
Kigelia pinnata

An Ethnobotanical and Scientific Review

Sausage Tree *Kigelia pinnata*. Photo ©2012 Simon Jackson

By Simon Jackson & Katie Beckett

Introduction

Southern Africa contains over 30,000 plant species, many of which have potential as economically useful plants that are relatively unknown to Western civilization due to past trade embargoes. In fact, only 50 of these species are currently traded to any significant degree.[1] A few hundred of these species are already known in preliminary research to have potentially beneficial biological activities. The scale of a potential marketing opportunity is large. With new ethnic ingredients in cosmetics and so-called cosmeceuticals being launched into the Western market, it is only a matter of time before African botanicals are targeted as potential sources of new drugs, cosmetics, and cosmeceuticals by members of industry.

One native African plant with great marketing potential is the sausage tree (*Kigelia africana*; syn. *K. pinnata**). *Kigelia* is now generally considered to be a highly variable monospecific genus of the family Bignoniaceae. Although several species have been reported in the past, they are also synonomous with *Bignonia africana*, *K. abyssinica*, *K. acutifolia, K. aethiopum*, *K. africana, K. ellioti*, *K. elliptica*, *K. impressa*, and *K. spragueana*. The aim of this article is to review the ethnobotanical uses and scientific research regarding this useful plant.

*As with most botanical nomenclature, there are several scientific names for the same plant. In the American Herbal Products Association's *Herbs of Commerce*, 2nd edition—the primary reference *HerbalGram* uses for Latin binomials—the preferred binomial for sausage tree is *Kigelia africana*. The same is true in other taxonomic resources, The Plant List and the United States Department of Agriculture's (USDA) Germplasm Resource Information Network (GRIN), with *Kigelia pinnata* listed as a synonym. The author of this article has preferred to use *K. pinnata*.

Nomenclature and Botanical Description

The adult sausage tree has spectacular fruits; these can weigh several kilograms and resemble large sausages, hence the tree's common English name. In Afrikaans, it is known as *worsboom*, *kalabasboom,* and *komkommerboom*; it is also known as *umfongothi* (Zulu), *muvevha* (Venda), and *mvunguti* (Chichewa-Malawi). It is a semi-deciduous-to-deciduous tree that grows up to 25 meters tall. It can be found all over sub-Saharan Africa, but its native range extends from Tanzania in the north to KwaZulu–Natal in South Africa in the south**.** Its habitat includes open woodlands and moist places such as riverbanks on alluvial soils, but is widespread throughout the savannah areas of tropical Africa. (See map 1)

The tree's bark is grey and smooth and flakes in older specimens. Leaves are crowded near the tips of branches, and young leaves are brownish red. Flowers bloom in long, loose, pendulous sprays of 5-12 flowers. Petals are a deep, velvety red with yellow veining on the outside. The cylindrical fruit is pendulous on a long fruit stalk. The fruit can grow up to 1 meter long and 20 cm wide and is grey and rounded at the apex.

The tree flowers from August to October and fruits from December to June. Depending on the climate, the sausage tree is remarkably fast-growing and can mature in 4 to 5 years. Ripe fruits can weigh up to 12 kg and can cause considerable damage when they drop. With its fast growth rate, spreading canopy, and interesting flowers and fruit, *Kigelia* is a popular street tree in South Africa and is grown to provide shade in Australia. It can also be used successfully for bonsai; the thick stem makes for an attractive feature.[2]

Map 1. Distribution of *Kigelia pinnata* in Southern Africa

Courtesy of PhytoTrade Africa

Harvesting

Kigelia begin to flower from the age of 6 years. Mature fruits can be found on trees year-round, but fruit collected from the ground is often of poor quality as it is quickly infested with insects or consumed by animals and therefore not used by humans. Fresh fruit from the trees are used to produce dried fruit pulp which has a range of applications. Seed germination improves after 1 year of storage, which could be due to physiological dormancy or simply because the fruits are shed before the seeds are fully mature and continue their development on the ground naturally. Soaking the seeds in boiling water for 1 minute aids germination—an 80% success rate has been noted. Cuttings can also be used for propagation. Truncheons cut from the tree can be planted directly into soil and root readily. *Kigelia pinnata* is pollinated by bats, but insects are also attracted to the flowers' color and fragrance.

The trees are normally found on flatlands which have a high water content (alluvial soils), and are periodically flooded, thereby often rendering them unsuitable for farming other crops. This benefits the *Kigelia* trees because it prevents large losses of the higher diameter fruit, as harvesting from flooded plains can become difficult. This flooding rescues trees from damage by herbivores (*e.g.*, baboons, elephants) and allows for regeneration.

Collection

In Malawi, the fruit is collected by a company called TreeCrops with support from the local community. Only fruit from trees within the forest areas are collected to avoid contamination, as TreeCrops regards farmlands as areas not suitable for sustainable collection and tries to preserve the organic agricultural status of the wild-harvested *Kigelia* fruit. The forest areas are established by the local community and mapped and monitored by TreeCrops. The land use is contracted for a period of at least 3 years to maintain the vegetation status and the forest ecology dynamics.

Harvestable Yields

During trials, TreeCrops established an average weight per fruit of 4.5 kg. Counts of the fruit per tree gave large variations between those not bearing fruit and those with over 200 fruits per tree. The average number was 41 fruits, meaning approximately 185 kg of fruit can be harvested per tree.

Sustainability Indicators

Annual assessments are carried out on the sustainable harvestable yield per tree. The average figure is multiplied with the number of trees per registered forest area and compared with the market demand. The real threat to sustainability is not over-harvesting from the tree, but the influence of humans—particularly grazing of wildstock, wildfires, and woodland destruction, as farming poses a threat to the natural vegetation. It is hoped that via TreeCrops and the local community,

poisonous. It has also been alleged that a woman died 36 hours after vomiting when this plant was used as an abortifacient. Additionally, *Kigelia* is used in beer to enlarge the sexual organs and reports exist of use for criminal poisoning.[12]

Non-Medicinal Uses

While baboons are known to eat the fruits, the pulp of unripe fruits are said to be posionous to humans. However, slices of mature baked fruits are used to ferment and flavor traditional African beer.[13] The seeds of ripe fruits can also be roasted in warm ash and consumed and are reported to be energy-rich, with significant amounts of phosphorous, protein, and lipids. In turn, the seed oil is rich in oleic acid and essential fatty acids, and has potential to be an important nutritional resource.[14] Additionally, the leaves of *K. pinnata* have been positioned as an important nutritional resource, comparable to other green leafy vegetables such as spinach.[15] They are consumed by lactating women in various parts of sub-Saharan Africa as they are thought to enhance the volume and quality of breastmilk. The dried leaves contain levels of essential amino acids that may provide beneficial health benefits as well as other minerals and nutrients including calcium, magnesium, and iron.[15]

The flowers are eaten by domestic stock and game, kudu, nyala, impala, and grey duiker. Leaves are consumed by elephants and kudu. The tree produces good quality timber and the wood is reported to be easy to work with. People living along large rivers, especially the Chobe and Zambezi, make their dugout canoes from the tree.[16]

The boiled fruits are also used to produce a red dye and the roots are reported to produce a yellow dye.[5] Much of the traditional use of *K. pinnata* surrounds topical application to the skin. It is reported that the Tonga women of the Zambezi Valley regularly apply cosmetic preparations of the fruits to their faces to maintain a blemish-free complexion.[5] Although not fully identified, this traditional use, like many others, is linked to the bioactive components of *K. pinnata*.

Chemical Constituents

It is always important to understand what secondary metabolites are found in a plant as they may form the basis for its traditional use, particularly if they are the same as, or similar to, compounds from other species. The family Bignoniaceae, of which *K. pinnata* is a member, is noted for the occurence of many secondary metabolites including iridoids, naphthoquinones,[17] saponins, tannins, flavonoids, coumarins, and several others, and is said to be an important source of bioactive compounds.[18] The roots and bark of *K. pinnata* have the naphthoquinone lapachol and the dihydroisocoumarin kigelin as major compounds.[19,20] Several other compounds, including the naphthaquinoids kigelinone, pinnatal, and isopinnatal, and the sterols stigmasterol and beta-sitosterol have been isolated from the bark.[20] The flavonoids 6-hydroxyluteolin-7-alpha-glucoside and luteolin have been isolated from the fruits and the leaves [21] while the roots have also yielded dihydroisocoumarins, lapachol, and sterols, and the presence of iridoid glycosides also has been reported.[19,22,23] Additionally, a study of the heartwood identified the presence of lapachol, dehydro-alpha-lapachone, tecomaquinone-I, D-sesamin, paulownin, kigeliol, kigelinone, β-sitosterol, and stigmasterol.[24]

Iridoids

The iridoids found in *Kigelia* correspond to the 9-carbon skeleton type, *e.g.,* catalpol, found in other members of the Bignoniaceae family. The major iridoids found in the root bark and stem bark of *K. pinnata* are specioside, verminoside, and minecoside.[25] These iridoids, specifically verminoside, have had the most scientific literature published on their unique anti-inflammatory properties. *In vitro* assays showed that verminoside had significant anti-inflammatory effects and inhibited both iNOS (nitric oxide synthase) expression and NO (nitric oxide) release in macrophage cell lines.[26,27,28] Further research also was undertaken *in vitro* on the cytotoxicity and cutaneous irritation of *Kigelia* fruit crude extract on skin cells grown in monolayers (ML) and in reconstituted human epidermis (RHE, 3D). These tests found that neither the iridoids verminoside nor verbascoside extracted from the fruit of the plant caused any release of pro-inflammatory mediators, and no histomorphological changes were noted of the RHE,[29] further suggesting anti-inflammatory activity.

Antiamoebic properties of iridoids also have been reported.[30] Extracts from the stem bark of *K. pinnata* were tested *in vitro* against *Entamoeba histolytica*. Butanol extracts from the *K. pinnata* stem bark showed *in vitro* antiamoebic activity. Three known iridoids—specioside, verminoside and minecoside—were isolated from stem bark and tested in isolation, and verminoside was shown to have a 2-fold antiamoebic activity as compared to a standard drug (metronidazole).[30]

Further analysis of the fruits by scientists in Egypt has identified 4 new iridoid compounds and 7 compounds already known.[31] A new furanone derivative formulated as 3-(2'-hydroxyethyl)-5-(2"-hydroxypropyl)-dihydrofuran-2(3H)-one, and 4 new iridoids named 7-hydroxy viteoid II, 7-hydroxy eucommic acid, 7-hydroxy-10-deoxyeucommiol, and 10-deoxyeucommiol have been isolated together with 7 known iridoids, jiofuran, jioglutolide, 1-dehydroxy-3,4-dihydroaucubigenin, des-p-hydroxybenzoyl kisasagenol B, ajugol, verminoside, and 6-trans-caffeoyl ajugol.

Phenylpropanoid and Phenylethanoid Derivatives

Further phytochemical investigation of the fruits of *K. pinnata* has yielded a new phenylpropanoid derivative identified as 6-*p*-coumaroyl-sucrose together with 10 known phenylpropanoid and phenylethanoid derivatives and a flavonoid glycoside. Compounds identified were 6-*O*-caffeoyl-β-D-fructofuranosyl-(2-1)-α-D-glucopyranoside 2-(3-hydroxy-4-methoxyphenyl) ethyl *O*-α-*L*-rhamnopyranosyl-(1-3)-[β-D-gluco-pyranosyl-(1-6)]-(4-*O*-feruloyl)-β-D-glucopyranoside, decaffeoylacteoside, acteoside, isoacteoside, jionoside D, echinacoside, 6-caffeoylglucose, and 6-feruloylsucrose while a flavonoid glycoside was identified as isoschaftoside.[32]

Naphthoquinones

In some South American species of Bignoniaceae, naphthoquinones are present in quite large amounts and influence the color of the wood. Lapachol was identified within root and bark extracts.[19] The characteristic compound of several species of *Tabebuia,* a related genus of the Bignoniaceae in the Western Hemisphere (mainly South America), lapachol is known to be cytotoxic and at one time was investigated as a potential treatment for cancer by the National Institutes of Health in the United States. Lapachol has been reported as present in small amounts in the wood and roots of *K. pinnata* by several investigators.[17] Two pairs of monoterpenoid-naphthaquinoid compounds—named pinnatal and isopinnatal—and kigelinol and isokigelinol, unique to *K. pinnata,* have been isolated from the roots and fruit of the plant.[33]

Sausage Tree *Kigelia pinnata*. Photo ©2012 PhytoTrade Africa

Coumarins

Researchers in India [17,19] identified and isolated from the root and the bark of *K. pinnata* 2 new dihydroisocoumarins: kigelin, and *O*-methylkigelin.

Flavonoids

The flavonoids 6-hydroxyluteolin-7-alpha-glucoside and luteolin have been isolated from the fruits and the leaves.[21] The flavonol quercetin and 4 flavonones, luteolin, its 6-OH analogue, and corresponding 7-O glucosides, were isolated from the leaves and fruits of *K. pinnata*.

Fatty Acids

Palmitic acid, already known to possess antibacterial activity, was identified in the fruit extract of *Kigelia*.[34]

Lignans

The lignan kigeliol was isolated from the wood and was the only lignan reported until 1999, when the neolignan balanophonin was isolated from the stembark.[17]

Steroids

The common steroids β-sitosterol and stigmasterol have been isolated by various workers from the bark and the root.[17]

Biological Activities

Most, if not all, of the experimentally demonstrated biological activity of *K. pinnata* has been connected in some way to its traditional uses.

Cytotoxic Activity

Anecdotal reports allege that applications of ethanolic extracts from the fruit have shown remarkable effects on solar hyperkeratoses and simple warts. The napthaquinoids norviburtinal and isopinnatal have been shown to inhibit cancer cell growth in culture.[35]

Based on the anecdotal reports of anti-melanoma activity, crude dichloromethane extracts of *K. pinnata* stem bark and fruit were tested and showed cytotoxic activity *in vitro* against cultured melanoma and other cancer cell lines.[4,10,35,36]

The dichloromethane extract of stem bark had been tested previously and found to give IC_{50} values between 2 and 5 µg/ml and, in this study, a similar extract also gave IC_{50} values between 1 and 4 µg/ml.[35] (See Table 1E online†)

The US National Cancer Institute (NCI) has recommended that if the IC_{50} value is less than 4 mcg/ml, then the extract/compound can be considered as having a cytotoxic effect. It is therefore apparent that these extracts possess such activity and that the activity of some of the fractions makes them candidates for further investigation. It appears that the extracts contain more than one active compound since activity of less than 4 mcg/ml was displayed by several fractions.[35] (See Tables 1E and 2E online†). Furthermore, work published by the Centre for Cancer Research and Cell Biology at Queen's University, Belfast, Ireland, reports that of the compounds identified and linked to cytotoxicity against human melanoma cells, furo-naphthoquinones were found to be the most potent. These compounds also demonstrated a cytotoxic effect in 2 human breast cancer cell lines; the authors suggest follow-up research into the impact of further modifications of the isocoumarin and furo-naphthoquinone moieties.[37]

The fractions B4 and F4 (See Table 1E†) were selected for further investigation and isolation of constituents since they showed the greatest and most consistent cytotoxic activity in all the melanoma cell lines tested. Thin-layer chromatography (TLC) examination of fractions of both stem bark and fruits contained the same 2 prominent zones, isolated and characterized as norviburtinal, isopinnatal, and beta-sitosterol.

Beta-sitosterol was shown by TLC to be present in all the active fractions, but it displayed little activity when tested and thus is unlikely to be responsible for the activity shown. Norviburtinal showed a much greater cytotoxic effect but showed little selectivity toward melanoma cell lines. Isopinnatal displayed slightly greater cytotoxic activity against the melanoma cell lines,[35] but its high cytotoxicity against the non-cancer fibroblasts indicates that it probably has a general cytotoxic effect that precludes it from being considered as a lead molecule for novel anticancer agents (see Tables 1E and 2E†).

If norviburtinal is the major cytotoxic compound present in the fractions, then its concentration should approximate to the IC_{50} value of the fraction

Sausage Tree *Kigelia pinnata*. Photo ©2012 Marius Els

ree *Kigelia pinnata*.
12 Simon Jackson

tumorgenesis model. It would seem that these results are starting

nacological uses of the

ncer and edema in the

.

icago's NAPRALERT
. pinnata's, stem, fruit,
nent of cancer of the

ve shown antinociceptctivites of *K. pinnata*
K. pinnata fruit exhibactivity on the tested
act produced a signified by acetic acid, an
hot-plate method, and
lin pain test in mice.
ta fruit also produced
nduced paw edema in
traditional use of *K.*
l inflammatory condithe anti-inflammatory
icted to the fruits as
of the flower has also
citivites.[41]
so displayed marked
ory effects in female
as reflected by a signifibition of the increase
paw circumference of
nd 54%, which was
y a subplantar injecn agg albumen.

Recent studies also have investigated the link between inflammatory disorders and male infertility, where application of *K. pinnata* fruit extract was found to decrease testicular and seminal fluid oxidative stress, suggesting *Kigelia*'s potential to increase fertility.[42] To fully understand the mechanisms involved, further research is required, but the studies, once again, provide a scientific basis for traditional use of this species.

Wound Healing

There is a long history of use surrounding *K. pinnata* and wound healing, particularly in relation to burns and bacterial infections. Aqueous stem bark extract applied to wound models supported this traditional use by showing an increased rate of wound contraction compared to the control.[43] The activity is presumably due to the free radical scavenging properties of the stem bark including the presence of β-sitosterol, an active compound in *K. pinnata*.[43,44]

Antimicrobial Activity

Traditionally, the use of the *K. pinnata* bark in many parts of Africa is for the treatment of sexually transmitted diseases, so it is of great interest that crude aqueous extracts from the stem bark have shown significant antimicrobial activity against *Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus,* and *Candida albicans*.[45,46] This activity was partially accounted for by the presence of pure iridoids, minecoside 1, and specioside 2. Further work at the University of Natal, in Durban, South Africa, also has shown antibacterial activity against gram-negative and gram-positive bacteria.[34] A mixture of 3 fatty acids exhibiting antibacterial effects was isolated from the ethyl acetate extract of the fruits using bioassay-guided fractionation.

Palmitic acid, already known to possess antibacterial activity, was the major compound in this mixture. Among the various other studies on this topic, a recent publication demonstrated that all *K. pinnata* extracts tested showed mild antibacterial activity, and the highest inhibition was displayed by the chloroform-soluble extract against *Shigella boydii* and *Pseudomonas aeruginosa*.[47] The identification of the compounds involved in the activity is crucial if medicinal uses of *K. pinnata* are to be further developed.

The antibacterial activity of *K. pinnata* stem bark on *Salmonella* species was investigated and demonstrated 100% inhibition of the test organism at an extract concentration of 10% to 20% (v/v).[48] The anti-nutrients which may be reponsible for the inhibition include alkaloids, tannins, saponins, phenols, and flavonoids, all of which are present in *K. pinnata*.[48] The results of this particular study indicate the potential of *K. pinnata* extracts to be used in the treatment of infections caused by antibiotic-resistant *Salmonella* species.

Antidiarrheal Activity

Antidiarrheal activity has also been exhibited in experimental *in vivo* models. Aqueous leaf extracts were tested on mice. Evidence for antidiarrheal activity was provided by the reduced fecal output and protection from castor oil-induced diarrhea in the extract-treated animals. The extract remarkably decreased the propulsive movement of the gastrointestinal contents. On the isolated guinea pig ileum, the extract did not appreciably affect acetycholine- and histamine-induced contractions, but significantly reduced nicotine-evoked contractions. The intraperitoneal LD_{50} of the extract in mice was estimated at 78.65±24 mg/kg.[26]

Antimalarial Activity

The World Health Organization has estimated that about 80% of the world's population in developing countries use herbal remedies to treat various ailments, and one of the world's biggest issues is treatment of malaria.[49] It is no surprise that the local populations in Africa use a concoction of several plant species, one being *K. pinnata*.[50] Researchers in Tanzania investigated the management of malaria with traditional herbal remedies, including the use, preparation, and administration by traditional healers in Tanzania. The results showed that all traditional healers treat malaria with herbal remedies consisting of 1-5 different plants, one of those being *K. pinnata*. Further work undertaken at the University of California-Berkeley has shown that the naphthoquinones extracted from the root extract of *K. pinnata* were highly effective against the malaria-causing protozoa, *Plasmodium falciparum*.[33] The search for new antimalarial drugs is becoming increasingly important as malarial parasites become more resistant to conventional treatments. Due to the positive results of *K. pinnata* preliminary trials, compounds from this species represent an interesting lead in the development of drugs and combination therapies against malaria.[33,51] One compound of particular interest in this field is specioside which has shown high activity as an antiplasmodial ingredient. Further work is required in this area to investigate drugs and compounds in combination and their potential toxicity.[51] Although specioside and *p*-hydroxycinnamic acid were found to be non-cytotoxic, 2 compounds present in an n-hexane extract, atranorin and 2β, 3β, 19α-trihydroxy-urs-12-en-28-oic acid, did show cytotoxity at high concentrations.[52]

Hepatoprotective Activity

Recent studies have been undertaken on *K. pinnata* and its potential hepatoprotective properties. Paracetamol (acetaminophen) is a widely used over-the-counter analgesic and antipyretic drug, and large doses can result in liver damage (hepatic necrosis). Studies performed *in vivo* on the protective effects of administration of extracts of *K. pinnata* on induced liver damage in mice showed that it was able to act as a hepatoprotective against paracetamol toxicity and that the mechanism by which it does this is by acting as an antioxidant.[53,54]

African Trypanosomiasis (Sleeping Sickness)

Human African trypanosomiasis, otherwise known as sleeping sickness, is a parasitic disease of people and animals caused by protozoa of the species *Trypanosoma brucei* and transmitted by the tsetse fly. It is a huge medical problem in Africa; research undertaken has shown that extracts from the root and stem bark of *K. pinnata* were active against *T. brucei*. Further activity-guided fractionation led to the isolation of 4 napthaquinoids, namely isopinnatal, kigelinol, isokigelinol, and 2-(1-hydroxyethyl)-naptho[2,3-b]furan-4,9-quinone, the most active compound being the furano-naphthoquinone structure.

Sustainability

One organization dedicated to the sustainability and scaleability of African botanicals is PhytoTrade Africa (www.phytotradeafrica.com). This nonprofit trade organization, which represents various natural products producers in the southern Africa region, states that the global natural products industry—including the key sub-sectors of food and beverages, cosmetics, herbal medicine, and pharmaceuticals—is currently valued at $65 billion USD per annum and is booming with a 15-20% annual growth rate in the last few years.[55] The current (as of October 2010) formal natural products trade in the southern Africa region is estimated at only $12 million USD per annum, although it may have the potential to grow to $3.5 billion USD per annum (data are based on author's presentation at the United Nations Food and Agricultural Organization in October 2010, in Harare, Zimbabwe). The market appears to be set for steady long-term growth, and tapping into this market is attractive for several reasons, particularly in the number of beneficiaries and their location in areas of low agricultural and economic productivity. The sausage tree is only one such example of a raw natural African botanical that could unleash a whole range of useful extracts, chemicals, and drugs for use in numerous markets.

PhytoTrade Africa, along with its members and partner organizations, works to develop sustainable, ethical, and traceable supply chains for key indigenous African plant products. The introduction of the PhytoTrade Africa Ethical Biotrade Charter enables members to embark on a path of continuous improvement with regards to environmental and social practices, and highlights PhytoTrade's commitment to fair and ethical trade, while simultaneously promoting biodiversity conservation. Important aspects of the Charter include sustainable resource use and harvesting practices, benefit-sharing agreements, and compliance with national and international legislation. Building capacity of harvesters is fundamental and is supported through a process of good-harvesting practices, including the development of transparent and sustainable business relationships between harvesters, manufacturers, and consumers of natural plant ingredients.

Two member organizations that work under the PhytoTrade Africa charter and supply extracts of *Kigelia* are Afriplex (Pty)Ltd (www.afriplex.co.za) and Blue Sky Botanics (www.blueskybotanics.com).

Conclusion

There are many anecdotal medicinal claims for the sausage tree,[2,3,6,16,46,56] and scientific research has identified several interesting compounds, many of which are known to have anti-micro-

Sausage Tree *Kigelia pinnata.* Photo ©2012 Simon Jackson

Potential Commercial Applications for Sausage Tree Extracts

The potential commercial applications for fruits of the sausage tree could include the following :

- Anti-inflammatory agent[29,40]– Possibly due to the iridoids having anti-inflammatory effect
- Sun creams[35] – Potential anti-cancer (melanoma activity)
- Anti-Eczema – Anecdotal reports on use against eczema
- Anti-Psoriasis – Anecdotal reports on use against psoriasis
- Breast-firming creams – Traditional uses and skin tightening properties
- After-sun lotions – Anecdotal report on treatments of solar keratosas (napthaquinones)
- Cosmetics/Cosmeceuticals – Skin tightening, anti-inflammatory, even skin tone and blemish-free skin
- Anti-microbial moisturizing[34,45,46] – Possibly due to iridoids, minecoside 1, and specioside 2, and presence of fatty acids, giving anti-microbial activity
- Anti-malarial agent[50] – Research suggests that *Kigelia* is used as an anti-malarial locally in Africa
- Anti-bacterial agent[34,60] – Potentially due to fatty acids
- Anti-molluscidalagent[26, 30] – Potentially due to anti-amoebic activity of iridoids

bial,[30] anti-inflammatory,[29,40] anti-fungal, antibacterial,[27] and cytotoxic activity.[35,36,57] Obviously, additional research is required to determine the modes of action and disease states upon which these compounds show activity. Nevertheless, *K. pinnata* remains an interesting plant for further research into novel agents for the dietary supplement, pharmaceutical, cosmetics, and so-called "cosmeceutical" industries.

Commercial *Kigelia* preparations for treating the skin are marketed in South Africa, but no medical claims are made. However, it is widely believed that these creams reduce pigmentation in freckles and help sores to heal, the latter effect possibly being related to traditional wound-healing and antibacterial components. In Europe and Asia, the traditional claims for bust-firming and skin-tightening have been used in many commercial applications and skin-care products are available in these markets.

However, from a commercial standpoint, it would seem that efforts to address the twin goals of environmental sustainability and economic development in southern Africa regarding African botanicals have only just begun.[55] Work performed in Uganda has highlighted that prioritization and domestication of key medicinal plant species must be undertaken, and a survey in 2004 nominated *K. pinnata* as a key species for domestication for future use as a medicinal crop.[58]

It is the aim of this article and all the cited references to provide an overview of the potential, current, and future contributions that *Kigelia*, and eventually other African plants, can make both internal to Africa and on the global stage. This is a message mirrored recently in the first chapter of a new book on African medicinal plants, *African Natural Plant Products: Discoveries and Challenges in Chemistry and Quality.*[59] HG

†Tables 1E, 2E, and 3E available online at http://cms.herbalgram.org/herbalgram/issue94/FEAT_sausagetree.html

Simon Jackson, PhD, is a pharmacognosist who earned his MPhil and PhD at Kings College, in Chelsea, London. His studies centered on African medicinal plants in the treatment of malignant melanoma and solar keratosis, and he worked alongside the melanoma unit at Charing Cross Hospital, Fulham, London. He performed his post-doctorate research at the Royal Botanic Gardens, Kew.

Among his many career accomplishments, Dr. Jackson has served as a pharmacognosy lecturer at University of Zimbabwe School of Pharmacy, and, in 2011, he worked on an African indeginous plants project sponsored by the Food and Agriculture Organization of the United Nations. He currently acts as a pharmacognosy consultant for a UK-based herb company. (Disclosure: Dr. Jackson has formulated a Kigelia *product that will launch this year through his own company, Dr. Jackson's Natural Products.)*

Katie Beckett received her First Class Honours Degree in Environmental Biology from Newcastle University, where she was also awarded for achievements in plant science. She was one of a team of three to undertake an expedition to the southern rainforests of Cameroon to map and record cultural and resource-based reliance on the forest by indigenous groups. Additionally, Beckett has co-authored several publications on natural plant products from Africa, including cosmetic, food, and herbal medicinal ingredients.

Beckett currently sits on the membership committee for the Union of Ethical BioTrade. She is employed as a research associate at PhytoTrade Africa, the natural products trade association for southern Africa. Her research focus ranges from the supply chain of natural plant products to plant chemistry to regulatory issues and market trends.

Acknowledgement

The authors wish to acknowledge Emeritus Professor Peter Houghton, whose example and expansive body of *Kigelia* research inspired this article.

References

1. Welford L, Le Breton G. Bridging the Gap: Phytotrade Africa's experience of the certification of natural products. *Forests, Trees and Livelihoods.* 2008;18:69-79.
2. Watt JM, Breyer-Brandwijk MG. *The Medicinal and Poisonous Plants of Southern and Eastern Africa*. 2nd ed. London, UK: Livingstone; 1962.
3. Jackson SJ, Houghton PJ, Photiou A, Retsas S. The isolation of a novel antineoplastic compound from a bioassay guided fractionation of stem bark and fruit extracts of *Kigelia pinnata* (Bignoniaceae). *Br J Cancer*. 1996;73(170):68.
4. Jackson SJ. Enlisting tree sausage in the war on cancer. *National Geographic.* 1995;188(2).
5. Saini S, H Kaur, et al. *Kigelia africana* (Lam.) Benth—An overview. *Natural Products Radiance.* 2009;8(2):190-197.
6. Gelfand M, Mavi S, Drummond RB, Ndemera B. *The Traditional Medical Practitioner in Zimbabwe*. Gweru, Zimbabwe: Mambo Press; 1985.
7. Oliver–Bever B. *Medicinal Plants in Tropical West Africa.* London, UK: Cambridge University Press; 1986.
8. Mabogo DEN. The ethnobotany of the Vhavenda. [Unpublished Master of Science thesis: University of Pretoria; 1990.]
9. Kokwaro JO. *Medicinal Plants of East Africa*. 3rd ed. Nairobi, Kenya: University of Nairobi Press; 2009.
10. Houghton PJ, Photiou A, Uddin S, *et. al.* Activity of extracts of *Kigelia pinnata* against melanoma and renal carcinoma cell lines. *Planta Med.* 1994;60:430-433.
11. Roberts M. *Indigenous Healing Plants*. Southern Book Publishers, Halfway House; 1990.
12. Vercourt B, Trump EC. *Common Poisonous Plants of East Africa*. London, UK: HarperCollins; 1969:210
13. Laswai H, Wendelin A, et al. The under-exploited indigenous alcoholic beverages of Tanzania: Production, consumption and quality of the undocumented "Denge." *African Study Monographs.*1997;18(1):29-44.
14. Chivandi E, Davidson B, et al. *Kigelia africana* seed: proximate,
29. Picerno P, Autore G, Marzocco S, Meloni M, Sanogo R, Aquino R. Anti-inflammatory activity of verminoside from *Kigelia africana* and evaluation of cutaneous irritation in cell cultures and reconstituted human epidermis. *J Nat Prod*. 2005;68:1610-1614.
30. Bharti N, Singh S, Naqvi F, Azam A. Isolation and *in vitro* antiamoebic activity of iridoids isolated from *Kigelia pinnata. ARKIVOC.* 2006;69-76.
31. Gouda Y, Abdel-baky A, Darwish F, Mohamed K, Kasai R, Yamasaki K. Iridoids from *Kigelia pinnata* DC. Fruits. *Phytochemistry.* 2003;63: 887-892.
32. Gouda Y, Abdel-Baky A, Mohamed K, Darwish F, Kasai R, Yamasaki K. Phenylpropanoid and phenylethanoid derivatives from *Kigelia pinnata* DC. Fruits. *Nat Prod Res.* 2006;20(10):935-939.
33. Malerich J, Trauner D. Biomimetic synthesis of Pinnatal and Sterekunthal A. *J Am Chem Soc.* 2003;125(32), 9554-9555.
34. Grace O, Light M, Lindsey K, et al. Antibacterial activity and isolation of active compounds from fruit of the traditional African medicinal tree *Kigelia africana*. *S Afr J Bot*. 2002;68:220-222.
35. Jackson SJ, Houghton PJ, Retsas S, Photiou A. In vitro cytotoxicity of norviburtinal and isopinnatal from *Kigelia pinnata* against cancer cell lines. *Planta Med.* 2000;66:758-761.
36. Fouche G, Cragg G, Pillay P, Kolesnikova N, Maharaj V, Senabe J. *In vitro* anticancer screening of South African Plants. *J Ethnopharmacol.* 2008;119:455-461.
37. Higgins C, T Bell, et al. Growth inhibitory activity of extracted material and isolated compounds from the fruits of *Kigelia pinnata*. *Planta Med.* 2010;76:1840-1846.
38. Azuine M, Ibrahim K, Enwerem N, Wambebe C, Kolodziej H. Protective role of *Kigelia africana* fruits against benzo[a]pyrene-
cytotoxicity of crude extracts and compounds from the stem bark of *Kigelia africana* (Lam) Benth (Bignoniaceae). *Parasitol Res.* 2011;108:1383-1390.
53. Olaleye M, Rocha B. Acetaminophen-induced liver damage in mice: Effects of some medicinal plants on the oxidative defense system. *Exp Toxicol Pathol.* 2008;59:319-327
54. Olalye M, Rocha J. Commonly used tropical medicinal plants exhibit distinct *in vitro* antioxidant activities against hepatotoxins in rat liver. *Exp Toxicol pathol.* 2007;58(6):433-438.
55. Sunderland T, Harrison S, Ndoye O. Commercialisation of non-timber forest products in Africa: history, context and prospects. In: Sunderland T, Ndoye O. (eds). *Forest Products, Livelihoods and Conversation: Case Studies on Non-Timber Forest Product Systems*. Vol 2 – Africa. Bogor, Indonesia: CIFOR. 2004;1-24
56. Retsas S, Photiou A, Jackson SJ. Pharmaceuticals from plants. *The Lancet.* 1994;344:8917.
57. Houghton PJ, Jackson S, Photiou A, Retsas S. Activity of extract of the fruit of *Kigelia pinnata* against cultured melanoma cells. [Abstract/Poster] Presented at UK Association of Pharmaceutical Scientists. Kings College London; November 18, 1994.
58. Katumba B, Boffa J, Abigaba G, Okorio J. Domestication of medicinal tree species in the Victoria lakeshore region. *UJAS.* 2004,9:84-88
59. Blumenthal M. African natural plant products: A foreword to the science and challenges. In: Juliani HR, Simon JE, Ho C-T. *African natural plant products: New discoveries and challenges in chemistry and quality*. Washington, DC: American Chemical Society, 2009.
60. Owolabi O, Omogbai E, Obasuyi O. Antifungal and antibacterial activities of the ethanolic and aqueous extract of *Kigelia africana* (Bignoniaceae) stem bark. *Afr J Biotechnol.* 2007;6(14):1677-1680.

Procter & Gamble Buys New Chapter, Inc.

New Chapter, Inc., a vitamin and supplement company based in Brattleboro, Vermont, announced in mid-March its purchase by Procter & Gamble, the world's largest consumer goods company, for an undisclosed price. New Chapter founders Paul and Barbi Schulick assured employees that the corporation plans to operate New Chapter as a wholly owned subsidiary with headquarters remaining in Brattleboro, and that no significant changes in jobs, compensation, benefits, or business practices will take place.

"Our shared mantra is acquisition, not assimilation," wrote the Schulicks in a company memo to New Chapter employees (e-mail to M. Blumenthal, March 16, 2012). "Our culture, guiding principles, and credo will not change and will only be buoyed by the superlative values gleaned from Procter & Gamble's resources and experience."

New Chapter embarked on its mission to harness the healing power of herbs in 1982. At the time, its liquid herbal extracts (originally sold under the name New Moon) were being pressed in a makeshift garage factory. Thirty years later, its purchase by Procter & Gamble signifies a new era in the company's history.

"There's probably no better evidence of mainstream consumer acceptance of the benefits of herbal dietary supplements than P&G's acquisition of New Chapter," said ABC Founder and Executive Director Mark Blumenthal in a Member Advisory sent to ABC members.[1] "Obviously, Procter & Gamble has done a significant amount of due diligence in researching not only New Chapter's history and product quality but also in determining the future growth potential for New Chapter's herbal and other dietary supplement products. A company like P&G doesn't make such a strategic move into a new area like dietary supplements without a considerable level of research."

The "Stonyfield Model"

Reminding consumers of past changes in the natural products industry, New Chapter Chairwoman Elizabeth Bankowski has said the company sees the transition "running along a Stonyfield model."[2] Stonyfield Farm, an organic yogurt company, was acquired by the French consumer products corporation Group Danone—owner of brands such as Evian® and Activia®—between 2001 and 2003.

"Typically, when a big conglomerate buys a smaller organic or natural-food company, the smaller company undergoes management changes," Stonyfield's website states in a section called "Our Extended Family."[3] "But Groupe Danone has allowed us to continue managing our company autonomously, and we've remained true to our mission."

Procter & Gamble's acquisition of New Chapter is the latest example of a large corporation purchasing a small, natural products company. In 1997, the natural, plant-based beauty care line Aveda was purchased by the global cosmetics manufacturer Estée Lauder. After more than a decade, "the smaller, environmental-focused personal care company has benefitted from the larger scale of its owner while also influencing Estée Lauder's sustainability efforts," GreenBiz.com reported in 2010.[4]

In a similar deal, the global consumer products giant Colgate-Palmolive purchased the natural personal care line Tom's of Maine® for $100 million in March 2006—less than a week after the international cosmetics and beauty company L'Oreal's acquired beauty products seller The Body Shop® for $1.1 billion.[5]

"We chose Colgate as our partner because they have the global expertise to help take Tom's of Maine to the next level," said Tom and Kate Chappell, co-founders of Tom's, in a company press release.[6] "Colgate has a commitment to product excellence, to global efforts to promote oral health and had a 200-year history of caring for consumers and for giving back to the community."

More recently, the Clorox Company—a business synonymous with its bleach products—purchased the natural personal care products line, Burt's Bees, for $913 million in 2007.[7] The *Nutrition Business Journal* (NBJ) noted that Clorox "wrote down the value of Burt's Bees by $250 million" after low sales numbers in 2011. However, the company's lifestyle division saw sales growth of 6% in the second fiscal quarter of 2012. Even with recent price increases throughout their product lines, Burt's Bees is still performing well, according to NBJ.[8]

Despite generally positive outcomes of past mergers, the Schulicks of New Chapter took measures to reassure customers after the announcement. On March 19, they posted an explanatory message to the company's Facebook page.

"Like many of you, at first this was hard to imagine but through many conversations about how they would manage our business, we reached the conclusion that their desire to 'do no harm' to New Chapter is real," they wrote.[9] "We hope you will not jump to conclusions and will instead give this venture the time it needs to prove itself. We have a high degree of confidence and we, and our diligent staff, will be vigilant to assure New Chapter remains faithful to its founding principles."

Two days later, after hundreds of continued comments, the Schulicks appeared in a YouTube video "to address customers who are concerned, skeptical, and angry—sometimes *very* angry—about what has occurred," Paul said in the video.[10] On New Chapter's Facebook page, most comments were pointedly negative, with many users vowing to stop purchasing New Chapter products after "selling out" to P&G. While many wrote that they were "stunned," "disappointed," and "disturbed" by the decision, others offered their support of the company's new direction.

The Schulicks have admitted that, on the surface, merging with one of the world's largest companies seems like an odd move for a "progressive, innovative, entrepreneurial company like New Chapter," which employs roughly 175 people in its Brattleboro facilities. However, they say it is rare to find a corporation that carries "the unparalleled commitment to quality, trust, and excellence that is foundational to Procter & Gamble."

"For us it's always been about healing, it's never been about the more business aspects," Barbi said in the video. "We needed other people to come in and help us with that part."

New Opportunities

The Schulicks will remain with New Chapter, but in different roles. Paul will serve as the executive vice-president of science and innovation and Barbi will become vice-president of organization and culture. Procter & Gamble's director of consumer and market knowledge, Kyle Garner, will join New Chapter as the new chief executive.[2]

In their memo to staff, the Schulicks wrote that Procter & Gamble has "the ability to turbocharge our mission while sustainably delivering the wisdom of nature to people and planet in ways we never even imagined." Additionally, the founders believe that harnessing the expertise of the 175-year-old company will allow New Chapter to better navigate complex regulatory process, strengthen "quality, supply chain, and science platforms," and enrich philanthropic and sustainability efforts.

New Chapter was awarded ABC's Varro E. Tyler Commercial Investment in Phytomedicinal Research Award in 2011.[11] It was the first American company to be honored with the award. New Chapter has sponsored research arrangements with institutions such as Columbia University, Cornell University, and the University of Texas M.D. Anderson Cancer Center in order to scientifically assess the beneficial qualities of some of its products, particularly the prostate health formula Zyflamend®, made with supercritical carbon dioxide extracts of various herbs.

Procter & Gamble, a Fortune 500 company based in Cincinnati, Ohio, markets a wide variety of products around the world from shampoo and razors to diapers and detergents, including such brands as Puffs®, Prilosec®, and Tide®. In 2011, Procter & Gamble reported more than $80 billion in sales. The purchase of New Chapter is the company's first venture into the vitamin and supplement markets, according to an article from *The Brattleboro Reformer*.[12]

However, Blumenthal added that "Procter & Gamble is no stranger to the herbal ingredients arena. They research and develop many botanical ingredients for a variety of consumer products that they sell in many parts of the world."[1]

The Schulicks say they are energized and inspired by Procter & Gamble's commitment to honoring the integrity of the company, while continuing to further their mission. "Procter & Gamble's investment in New Chapter is testament to the fact that the largest consumer goods company in the world now recognizes the power of nature's healing and believes in its promise to transform global health and wellness."

In New Chapter's recent YouTube video, Paul summarized his hopes for consumers. "The one thing I would ask you is to … take a deep breath with us and give us a little bit of time to prove ourselves."[10]

Both New Chapter and Procter & Gamble are long-time Sponsor Members of ABC. HG

—Tyler Smith

References

1. Proctor & Gamble Buys New Chapter, Inc. [member advisory]. Austin, TX: American Botanical Council, March 19, 2012.
2. Watson E. New Chapter: 'Countless opportunities await' under new owner, P&G. NutraIngredients-USA website. Available at: www.nutraingredients-usa.com/Industry/New-Chapter-Countless-opportunities-await-under-new-owner-P-G. Accessed March 19, 2012.
3. Our extended family. Stonyfield Farm website. Available at: www.stonyfield.com/about-us/our-story-nutshell/our-extended-family. Accessed March 24, 2012.
4. Aveda and Estee Lauder find common ground on sustainability. GreenBiz website. Avaialble at: www.greenbiz.com/news/2010/11/04/aveda-estee-lauder-find-common-ground-sustainability. Accessed March 24, 2012.
5. Howard T. Big companies by small brands with big values. *USA Today*. March 26, 2006. Available at: www.usatoday.com/money/companies/2006-03-21-natural-usat_x.htm. Accessed March 26, 2012.
6. Colgate purchasing Tom's of Maine: Enters fast-growing natural products segment. [press release]. New York, NY: Tom's of Maine; March 21, 2006.
7. Story L. Can Burt's Bees turn Clorox green? *New York Times*. January 6, 2008. Available at: www.nytimes.com/2008/01/06/business/06bees.html?pagewanted=all. Accessed March 25, 2012.
8. Burt's Bees and Gud to drive growth for Clorox. *Nutrition Business Journal*. February 8, 2012. Available at: http://newhope360.com/finance-and-investment/burts-bees-and-g-d-drive-growth-clorox. Accessed March 25, 2012.
9. A personal note from the founders of New Chapter. Facebook website. Available at: www.facebook.com/notes/new-chapter/a-personal-note-from-the-founders-of-new-chapter/10151409021285500. Accessed March 20, 2012.
10. A message from our founders. YouTube. March 22, 2012. Available at: www.youtube.com/watch?v=i-cgPvegoSQ. Accessed March 25, 2012.
11. American Botanical Council Announces Recipients of Botanical Excellence Awards. [press release]. Austin, TX: *HerbalGram*; March 11, 2011.
12. Weiss-Tisman H. P&G Buys New Chapter. *The Brattleboro Reformer*. March 17, 2012. Available at: www.reformer.com/localnews/ci_20194274/p-g-buys-new-chapter. Accessed March 19, 2012.

The Adulteration of Commercial "Grapefruit Seed Extract" with Synthetic Antimicrobial and Disinfectant Compounds

By John H. Cardellina II, PhD

Material called "grapefruit seed extract" (GFSE[1]) has been sold in the natural products market for 3 decades or more as an ingredient in or preservative for cosmetic and dermatological preparations and also in dietary supplements. GFSE, supposedly an extract of the seeds of the common grapefruit (*Citrus* x *paradisi,* Rutaceae), has been touted in popular literature as a natural antimicrobial agent for both topical and internal use, including, but not limited to, eczema, acne, cold sores, athlete's foot, sore throats, thrush, vaginal infections, colds, various gastrointestinal disorders and infections, allergies, and gingivitis.[2,3] Much of the commercially available GFSE is produced via proprietary methods that purportedly involve the use of catalytic processes and the addition of solvents and/or other chemicals. For example, in the case of one of the leading branded consumer products labeled as containing "grapefruit seed extract," this process has not been fully disclosed or explained in any publicly available literature, but is claimed to involve a multistep process that includes boiling ground, dried seeds and pulp in water, then "…distillation, catalytic conversion and ammoniation…"[4] to yield GFSE, the active ingredient of which "…is a quaternary ammonium chloride (a diphenol hydroxybenzene reacted with ammonium chloride) similar to benzethonium chloride…".[4]

In 1991, a collaboration led by Nishina (Food Research Laboratory, Nippon Oil and Fats Co.; Tokyo, Japan) published the first analysis of commercial GFSE and reported that preparative high-performance liquid chromatography (HPLC) led to identification of methyl *p*-hydroxybenzoate, a preservative, and triclosan, a microbicide and disinfectant.[5] Five years later, Sakamoto *et al*., at the Japanese National Institute of Health Sciences in Tokyo, repeated the analysis of GFSE using HPLC-ESIMS (HPLC with electrospray ionization mass spectrometry), and compared the commercial GFSE with ethanolic extracts of grapefruit seeds that they prepared themselves.[6] Like the Nishina *et al*. study, Sakamoto found methyl *p*-hydroxybenzoate and triclosan as 1.66% and 1.97% of the GFSE, respectively; perhaps more importantly, no trace of these compounds was found in their ethanolic extract of grapefruit seeds. Unfortunately, these 2 important papers may not have received the level of attention they deserved because they were published in Japanese-language journals and went largely unnoticed outside of Japan.

However, at least 2 groups did take note of Sakamoto's report. The von Woedtke group (Ernst Moritz Amdt University; Greifswald, Germany) analyzed 6 commercially available GFSE extracts; five of them exhibited significant antimicrobial activity. The 5 antimicrobial GFSE extracts were found by TLC (thin-layer chromatography) to contain the synthetic microbicide benzethonium chloride; three of those also contained triclosan and methyl *p*-hydroxybenzoate.[7] The one remaining GFSE product and fresh extracts prepared from grapefruit seeds with glycerol, water, ethanol, and combinations of the three, contained none of the 3 synthetic preservatives/disinfectants, nor did any of these samples exhibit any antimicrobial activity. Thus, there was a direct correlation of the presence of synthetic preservatives, disinfectants, and microbicides with the antimicrobial activity observed in the GFSE products.

Takeoka's group at the USDA (Western Regional Research Center; Albany, California) subsequently published 2 analyses of GFSE formulations.[8,9] In the first, they analyzed what the authors noted to be two of the leading commercial GFSE products in the United States, one a liquid concentrate and the other a concentrated powder, by a combination of extraction, HPLC-ultraviolet spectroscopy (HPLC-UV), mass spectrometry (MS), and nuclear magnetic resonance spectroscopy (NMR). Rather than methyl *p*-hydroxybenzoate and triclosan, they found benzethonium chloride as 8% of the mass of the liquid GFSE sample. Benzethonium chloride was also found in the concentrated powder, but was not quantified. Later, Takeoka *et al*.[9] examined the contents of the same commercial product analyzed by Nishina *et al*.[5] by HPLC combined with ESIMS and ESIMS/MS, but they found no triclosan, methyl *p*-hydroxybenzoate, or benzethonium chloride. Instead, they found a mixture of benzalkonium chlorides as an astonishing 22% of the extract weight. These studies prompted even broader surveys of GFSE preparations and products containing them.

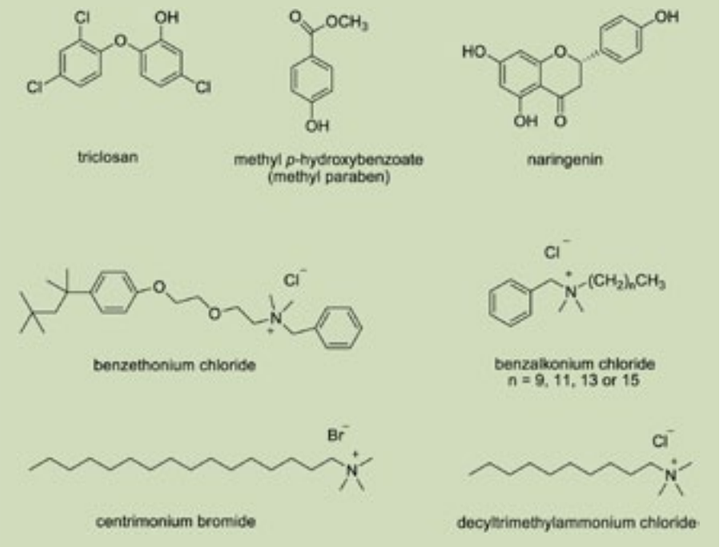
Avula *et al*. developed an HPLC-UV-MS method for the simultaneous identification and quantification of benzethonium chloride, methyl *p*-hydroxybenzoate, and triclosan in GFSE products and used it to evaluate 9 unidentified commercial GFSE products, one pomegranate (*Punica granatum*, Punicaceae) seed extract, and a freshly prepared methanolic extract of grapefruit seeds.[10] No methyl *p*-hydroxybenzoate was detected in any sample; triclosan was detected in 3 of the commercial GFSE preparations (0.009-1.13%); and benzethonium chloride was found in 8 of 9 commercial GFSE preparations—one below the limit of quantification, one at 0.29%, and the other six at 5.97-21.84% of the mass. The commercial pomegranate seed extract (used as a control) and the fresh grapefruit seed extract were devoid of all 3 compounds.

Ganzera *et al*. (University of Innsbruck, Austria) developed and validated an HPLC-UV-MS method for simultaneous determination of 18 possible preservatives, disinfectants, and microbicides in GFSE and tested 9 unidentified commercial products used for eco-farming—8 liquids and 1 powder.[11] All the products except 1 liquid claimed GFSE as a component of the product. The non-GFSE product contained none of the 18 possible contaminants, but 6 of the remaining 7 products contained between one and five of the analytes (Table 1). The liquid GFSE preparation contained methyl *p*-hydroxybenzoate (0.31%), benzoic acid (0.13%), methyl benzoate (0.05%), propyl *p*-hydroxybenzoate (0.12%), C_{12} benzalkonium chloride (3.47%), C_{14} benzalkonium chloride (1.15%), and C_{16} benzalkonium chloride (0.31%).

Table 1: Results of Analysis of GFSE Liquid Products by Ganzera *et al.*[11]

Contaminant/Adulterant	No. of products	Range of concentration
methyl *p*-hydroxybenzoate	2 products	9.88-17.89 mg/mL
propyl *p*-hydroxybenzoate	2 products	4.97-9.13 mg/mL
benzethonium chloride	4 products	2.48-176.90 mg/mL
C_{12} benzalkonium chloride	2 products	99.38-167.15 mg/mL
C_{14} benzalkonium chloride	2 products	33.86-69.07 mg/mL
C_{16} benzalkonium chloride	1 product	4.96 mg/mL

Figure 1. Structures of the Principal Disinfectants/Microbicides Found in Products Labeled "Grapefruit Seed Extract," and the Structure of Naringenin, the Most Abundant Flavonoid in Grapefruit.



Spinosi *et al*. (Istituto Zooprofilattico Sperimentale dell' Abruzzo e del Molise 'G. Caporale'; Teramo, Italia) used gas chromatography-mass spectrometry (GC-MS) to examine 17 GFSE products used as "organic" treatments of diseases of honey bees and found benzethonium chloride (0.003-21.5% in 14 products), cetrimonium bromide (3.202-11.656% in 5 products), and decytrimethylammonium chloride (10.32% in 1 product).[12] Their results suggested a strong correlation between the presence of chemical additives (disinfectants) and observed antimicrobial effects.

Sugimoto *et al*. (National Institute of Health Sciences; Tokyo, Japan) used HPLC-MS and ^{1}H-NMR to analyze 13 GFSE products used as food additives from 6 manufacturers, 5 dietary supplements from 4 manufacturers, 16 cosmetic products from 10 manufacturers, and 7 disinfectant or deodorant sprays from 7 manufacturers for the presence of the synthetic disinfectants benzethonium and benzalkonium chlorides.[13] Twelve of the food additive GFSE products contained one of the synthetic disinfectants—11 contained benzalkonium chloride and one contained benzethonium chloride (39.06%). The 3 concentrated liquid products with benzalkonium chloride contained 12.156-13.898% of the disinfectant; the other 8 products were dilutions or formulations made with one of the concentrated liquids containing 0.007-1.739% benzalkonium chloride. Two of the dietary supplements contained neither of the synthetic disinfectants, while the other three had benzethonium chloride in 0.008%, 0.215%, and 6.78 %, respectively. All of the cosmetic products contained benzethonium chloride (14.596-28.826%); one of them also contained 3.456% benzalkonium chloride. All of the disinfectant/deodorant sprays contained either benzalkonium chloride (0.014-0.208%) or benzethonium chloride (0.019-0.260%).

Bekiroglu *et al*. (Medical Products Agency; Uppsala, Sweden) subsequently developed and validated an NMR method for the quantitative analysis of benzethonium chloride in GFSE; they analyzed 3 unidentified commercial samples of GFSE and found 78 mg/mL of benzethonium chloride.[14]

The structures of the synthetic disinfectants and microbicides discussed herein are shown in Figure 1, along with that of naringenin, a flavonoid abundant in grapefruit.

In addition to the scientific studies cited above, the American Herbal Products Association (AHPA), a trade association representing the herbal industry in the United States, has repeatedly worked to draw attention to the problem of adul-

Grapefruit *Citrus* x *paradisi.* Photo ©2012 Steven Foster

terated GFSE via communications regarding recent GFSE publications to its industry members.[15,16,17] Further, Caldecott has published an essay on the subject, with emphasis on potential safety concerns about the adulterants that have been reported in commercial GFSE products.[18] To this author's knowledge, and based on extensive literature searches, there is no record of the medicinal use of grapefruit seed or grapefruit seed extract in any ancient or modern treatise on traditional herbal medicine, modern pharmacopeia, or other compilation of medicinal plants from any culture. A search of the PubMed database at the United States National Library of Medicine under the search term "grapefruit seed extract AND clinical trials" yielded no search results. [Search of www.pubmed.org, March 21, 2012.] The PubMed database, and others, do contain citations and abstracts of published reports on GFSE antimicrobial activity in experimental (*in vitro*) and *in vivo* animal models, but because the actual composition of such GFSE materials used in these studies was not clarified by accompanying chemical analyses, this entire body of research is questionable.

Conclusion

A significant amount, and possibly a majority, of ingredients, dietary supplements and/or cosmetics labeled as or containing grapefruit seed extract (GFSE) is adulterated, and any observed antimicrobial activity is due to synthetic additives, not the grapefruit seed extract itself. Tests conducted in multiple laboratories over almost 20 years indicated that all commercial GFSE preparations that exhibited antimicrobial activity contained one or more synthetic microbicides/disinfectants, while freshly-prepared extracts of grapefruit seeds made with a variety of extraction solvents neither exhibited antimicrobial activity nor contained the antimicrobial synthetic compounds found in the commercial ingredient materials. Furthermore, over the course of the 18 years covered by the various analyses, the actual antimicrobial compounds found in the putative grapefruit seed extracts changed from triclosan and methyl *p*-hydroxybenzoate in early samples to benzethonium chloride in the middle years to mixtures of benzalkonium and/or alkonium chlorides in more recent years. The suggestion on a commercial website[4] that these antimicrobial compounds are formed from the phenolic compounds naturally occurring in grapefruit seed and pulp by heating them with water, ammonium chloride, and hydrochloric acid is not supported by chemical evidence, or any known organic chemistry pathway. None of these compounds could be formed from flavonoids like naringenin, the most abundant flavonoid in grapefruit seeds, pulp, and peel, or other grapefruit seed constituents (*e.g.*, limonoids) and ammonium chloride; the alkyl chains and substituent arrays found in the antimicrobial adulterants are not naturally present in grapefruit seed and cannot be prepared from those materials**.** The fact that the antimicrobial components found in GFSE changed from 1991 to 2008 not only argues against such *in situ* synthesis (*i.e.*, occurring naturally or synthesized in the processing of grapefruit seed material itself), but is suggestive of efforts by manufacturers of these commercial materials to stay one step ahead of analytical methods to detect adulteration.

A significant amount, and possibly a majority, of ingredients, dietary supplements and/or cosmetics labeled as or containing grapefruit seed extract (GFSE) is adulterated, and any observed antimicrobial activity is due to synthetic additives, not the grapefruit seed extract itself.

Grapefruit *Citrus* x *paradisi*. Photo ©2012 Steven Foster

Safety Notes: A Swedish team has reported that a female (age not provided) on long-term warfarin (coumadin) treatment with regular monitoring consumed several drops of GFSE for 3 days. Three days later she developed a minor subcutaneous hematoma, at which time her INR (international normalized ratio, a measure of blood coagulation time) was found to be 7.9 (normal range for warfarin patients is 1-3). NMR analysis of the GFSE product she had been taking revealed the presence of water, glycerol, and benzethonium chloride. Benzethonium chloride was tested and found to be a potent inhibitor of the metabolizing enzymes CYP3A4 and CYP2C9. Inhibition of these enzymes results in prolonged, higher levels of circulating coumadin, thus increasing clotting times. The investigators (Medical Products Agency; Uppsala, Sweden) thus concluded that benzethonium chloride in the GFSE product consumed by the patient was responsible for the spike in her INR.[19]

A review of the Material Safety Data Sheets (MSDS) for the synthetic disinfectants and microbicides found in commercial samples of GFSE revealed a general pattern of eye, skin, and respiratory tract irritation, a few indications of genetic, developmental, or organ toxicity, and a moderate health hazard, although a few citations of more serious adverse effects were noted. A summary is provided in Table 2, below. HG

The fact that the antimicrobial components found in GFSE changed from 1991 to 2008 not only argues against such *in situ* synthesis (*i.e.*, occurring naturally or synthesized in the processing of grapefruit seed material itself), but is suggestive of efforts by manufacturers of these commercial materials to stay one step ahead of analytical methods to detect adulteration.

Table 2. Summary of Information from MSDS Sheets on Compounds Found in Commercial GFSE

Compound	HMIS[a]	NFPA[b]	Eye	Skin	Respiratory Tissue	Developmental or Genetic Toxicity	Other indication
triclosan	2	2	irritant	irritant	irritant	fetal death in rats after oral ingestion	
methyl paraben[c]	2	2	irritant	irritant	major irritant	NL[d]	
n-propyl paraben[c]	2	2	irritant	irritant	major irritant	NL[d]	
benzethonium chloride	2	2	irritant	irritant	irritant	sister chromatid exchange in hamster embryo	
benzalkonium chloride	3	3	burns	burns	destructive	NL[d]	toxic if ingested – nerves/liver
cetrimonium bromide	2	2	serious damage	irritant	NL[d]	NL[d]	
decyltrimethyl-ammonium chloride	NL[d]	NL[d]	irritant	irritant	irritant	NL[d]	

[a]Hazardous Material Identification System (2 = temporary or minor injury possible; 3 = major injury likely without prompt medical attention)
[b]National Fire Protective Association criteria (2 = temporary incapacitation or possible residual injury likely from continued or intense exposure without medical attention; 3 = serious temporary or residual injury possible from brief exposure, even with prompt medical attention)
[c]paraben = para-hydroxybenzoate
[d]Nothing Listed

John H. Cardellina II, PhD, is a natural product, organic, medicinal, and analytical chemist who has held positions in the pharmaceutical industry, academia, the National Cancer Institute, Office of Dietary Supplements, the US Army Research Institute of Infectious Diseases, and the Council for Responsible Nutrition. He is also a consultant in many areas of natural products research. Dr. Cardellina is the author or co-author of nearly 200 publications and co-inventor on numerous patents covering 13 classes of natural products and synthetic compounds. Among many organizational positions he has held, he is a past-president of the American Society of Pharmacognosy, a longtime member of the Advisory Board of the American Botanical Council, current Chair of the Board of Directors of the American Herbal Pharmacopoeia, Chair of the American Society of Pharmacognosy Foundation, and the book review editor for the Journal of Natural Products.

Acknowledgements

The author is deeply grateful to S. Matsunaga, PhD, for translating references 5, 6, and 13, and to S. Cardellina, MBA, for assistance with the translation of reference 12.

This article was peer reviewed by qualified experts in analytical chemistry and related disciplines, including some of the researchers whose papers are summarized and cited in this review.

Funding for the research, writing, editing, and peer review of this paper was made possible by a series of unrestricted educational grants made to the American Botanical Council for the ABC-AHP-NCNPR Botanical Adulteration Program. ABC, the American Herbal Pharmacopoeia, and the University of Mississippi's National Center on Natural Products Research are grateful for the support from a large group of underwriters, most of which are trade associations and companies that produce, supply, manufacture, and/or market herbal ingredients and/or products (current list is posted on the ABC website, www.herbalgram.org). The author of this review paper has no financial relationship with any of these underwriters.

References and Notes

1. Some of the papers cited in this article use the acronym GSE to refer to grapefruit seed extract. However, the author of this article prefers using the acronym GFSE for grapefruit seed extract to differentiate it from, and avoid confusion with, grape seed extract (from *Vitis vinifera*, Vitaceae), a widely used botanical product that is usually referred to as GSE. In an example of this potential (now realized) confusion, the authors of a recent paper on the pharmacological activity of grapefruit seed extract (Cao S, et al. A mitochondria-dependent pathway mediates the apoptosis of GSE-induced yeast. *PLoS ONE* 2012. 7: e32943) describe grapefruit seed extract as containing catechins and procyanidins, citing a reference to grape seed chemistry.
2. Sharamon S, Baginski BJ. *The Healing Power of Grapefruit Seed*. Twin Lakes, Wisconsin: Lotus Light Publications; 1997.
3. Sachs A. *The Authoritative Guide to Grapefruit Seed Extracts*. Mendocino, California: LifeRhythm; 1997.
4. Nutriteam.com. Citricidal Grapefruit seed extract. Available at: www.nutriteam.com/citricidal.htm. Accessed September 28, 2011.
5. Nishina A, Kihara H, Uchibori T, Oi T. Antimicrobial substances in"DF-100", extract of grapefruit seeds. *Bokin Bohai (J. Antibact Antifung Agents)* 1991;19:401-404. [commercial product identified in the paper]
6. Sakamoto S, Sato K, Maitani T, Yamada, T. Analysis of components in natural food additive "grapefruit seed extract" by HPLC and LC/MS. *Eisei Shikenjo Hokoku (Bull Natl Inst Health Sci.)*. 1996;114:38-42.
7. von Woedtke T, Schlüter B, Pflegel P, Lindequist U, Jülich W.-D. Aspects of the antimicrobial efficacy of grapefruit seed extract and its relation to preservative substances contained. *Pharmazie*;1999. 54:452-456. [commercial products identified]
8. Takeoka G, Lan D, Wong RY, Lundin R, Mahoney N. Identification of benzethonium chloride in commercial grapefruit seed extracts. *J Agric Food Chem.* 2001;49:3316-3320. [commercial products identified]
9. Takeoka GR, Dao LT, Wong RY, Harden LA. Identification of benzalkonium chloride in commercial grapefruit seed extracts. *J Agric Food Chem.* 2005;53:7630-7636. [commercial products identified]
10. Avula B, Dentali S, Khan IA. Simultaneous identification and quantification by liquid chromatography of benzethonium chloride, methyl paraben and triclosan in commercial products labeled as grapefruit seed extract. *Pharmazie*. 2007;62:593-596. Reference samples of all specimens tested are deposited at the Institute of Pharmacy, University of Innsbruck, Innsbruck, Austria.
11. Ganzera M, Aberham A, Stuppner H. Development and validation of an HPLC/UV/MS method for simultaneous determination of 18 preservatives in grapefruit seed extract. *J Agric Food Chem.* 2006;54:3768-3772.
12. Spinosi V, Semprini P, Langella V. Presence of chemical additives and microbial inhibition capacity in grapefruit seed extracts used in apiculture. *Veterinaria Italiana.* 2007;43:109-113.
13. Sugimoto N, Tada A, Kuroyanagi M, Yoneda Y, Yun YS, Kunugi A, Sato K, Yamazaki T, Tanamoto K. Survey of synthetic disinfectants in grapefruit seed extract and its compounded products. *Shokuhin Eiseigaku Zasshi*. 2008;49:56-62.
14. Bekiroglu S, Myrberg O, Ostman K, Ek M, Arvidsson T, Rundlöf, T, Hakkarainen B. Validation of a quantitative NMR method for suspected counterfeit products exemplified on determination of benzethonium chloride in grapefruit seed extracts. *J Pharm Biomed Anal* 2008;47:958-961.
15. Anon. Antiinfective compounds in grapefruit seed extract – not natural. *AHPA Report*. 2005; 20(7):12.
16. Anon. Adulteration of commercial GSE with synthetic preservative: nailed again. *AHPA Report.* 2005;20(9):10.
17. Anon. Grapefruit seed extract times three – the title says it all. *AHPA Report.* 2006;21(6):11.
18. Caldecott T. Grapefruit seed extract. *Medical Herbalism.* 2005;14:1-2.
19. Brandin J, Myrberg O, Rundlöf T, Arvidsson A-K, Brenning G. Adverse effects by grapefruit seed extract products in patients on warfarin therapy. *Eur J Clin Pharmacol*. 2007;63:565-570.

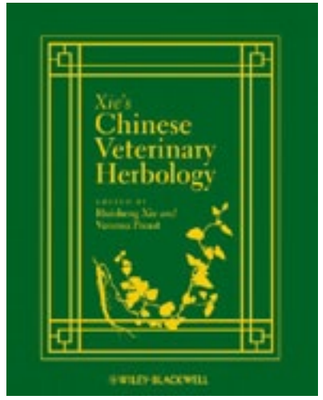
Xie's Chinese Veterinary Herbology by Huisheng Xie and Vanessa Preast (eds.); illustrated by Barbara Jean Beckford. Singapore: Wiley-Blackwell; 2010. Hardcover; 632 pages. ISBN: 978-0-8138-0369-2. $136.99.

As one of the most prolific teachers in the world of Traditional Chinese Veterinary Medicine (TCVM), Dr. Huisheng Xie has produced the first English language textbook of herbal medicine devoted solely to TCVM. This book is written as a text and reference for veterinarians who are studying or are already trained in the practice of TCVM. It is a valuable complement to his text on veterinary acupuncture, *Xie's Veterinary Acupuncture* (Blackwell, 2007). Contributing authors are mostly veterinarians but also include several MDs and OMDs; their origins range from the United States to Australia, China, and Korea.

The preface to the book states that it is intended to serve as a quick reference for practicing veterinarians and as a textbook for continuing education courses in TCVM. It does a very good job of meeting these goals, and as such is used by Dr. Xie's Chi Institute as a primary textbook for courses in TCVM. While there are many herbal reference texts for the TCM practitioner who treats human patients, the irrefutable "bibles" on the topic are the 2 Bensky texts: *Chinese Herbal Medicine: Materia Medica* (Eastland Press, 2004) and *Chinese Herbal Medicine: Formulas and Strategies* (Eastland Press, 2009). For the serious TCM student, veterinarian or not, these 2 texts remain the highest English-language authorities. However, for the veterinary herbalist, Dr. Xie's text deserves a place right next to them on the bookshelf and for many TCVM practitioners it will serve well as a single source.

A concise introductory chapter provides a general explanation of the principles of Chinese medicine and their applications in veterinary practice. General advice is provided on dosing and administration for small animals and equines. Lacking in this section is more species-specific information, such as dosing tips for cats and ruminants.

The bulk of the book is nicely organized into 3 sections. The first is a *materia medica*, which gives detailed information on individual herbs, grouped



by their functionality. For example: herbs to dispel damp, herbs to clear heat, and herbs to tonify deficiency. At the beginning of each section there is an introduction to the pattern being addressed and the observable clinical signs with each of these patterns. Tables are interspersed among the individual herb monographs, which summarize the patterns and the herbs most appropriate for use. The layout is similar to the Bensky text, providing for each herb the original reference text, part used, name, energy/taste, channel-organ, actions, form and preparation, dosage, cautions and contraindications, and side effects. Bensky also provides major chemical constituents, alternate species, local variants, and adulterants. While this additional information would make this text more complete, it would be more than what the average veterinary practitioner needs to have at his/her disposal. Information on known drug interactions would be useful.

Individual herbs are listed under headings organized by the genus name, followed by the Pinyin name. The name of each herb is given in the pharmacopeial, botanical, common, and Wade-Giles form. In addition, an English translation of the Chinese name is provided. In the case of several herbs that are quite common in Western herbal medicine, the common name provided is not the one most commonly used. For instance: *Prunella vulgaris* (Lamiaceae) is listed simply as prunella and not as self-heal. *Artemisia annua* (Asteraceae) is listed as artemisia and not as sweet-annie, and *Vitex agnus-castus (*Lamiaceae) is listed as vitex seed and not as chaste berry. In addition, the index does not include the common names which have been given. If one were to search using the common names for dandelion (*Taraxacum officinale*, Asteraceae), violet (*Viola sororia,* Violaceae), or Japanese honeysuckle *(Lonicera japonica*, Caprifoliaceae) using the index, they will not be found. Although the herbs are referenced in the text by these common names, they are indexed only under their genus and Pinyin names.

The *materia medica* chapters are graced with beautiful drawings by Barbara Beckford. These drawings are quite accurate and depict various parts of each plant including leaves, flowers, seeds, and roots. This is a great improvement over many Chinese herb texts which illustrate only the dried part used and not the entire plant. While photographs might be even more helpful, these drawings outshine those in Bensky's *Chinese Herbal Medicine: Materia Medica*. Unfortunately, illustrations are provided for only one-third of the herbs in the book. Hopefully, future editions will contain even more of them.

The second section of the text is devoted to Chinese veterinary herbal formulas. While Western herbal practitioners often utilize single herbs, or create their own customized blend of herbs, Chinese herbal medicine most often utilizes specific formulas that have been passed down through the centuries. Each formula is designed to treat a specific pattern of disharmony. While TCVM herbal practitioners may make minor adjustments to the proportions of herbs used, for the most part the formulas are still made in the traditional ratios, and they are presented here in such a way.

Herbal formulas are organized by chapters that describe their function, such as formulas to expel wind, formulas to eliminate dampness, and formulas to tonify deficiency. Each chapter begins with a brief explanation of the pattern addressed, and then lists the formulas in a well-organized fashion according to individual actions. For each formula, there is a detailed translation of the Chinese name and often an interesting story explaining the origins or history of the formula. Each formula description includes a table that lists ingredients, their relative quantities, and their primary actions within the formula. Analyses of each formula are quite detailed and provide a thorough explanation of the role of each individual herb. Information describing relevant clinical and pharmacological studies is provided for many of the formulas as well.

The information that is perhaps most useful in daily practice is the inclusion of "Dr. Xie's comments" for each formula, which refer to the specific veterinary uses of each formula. For example, in the case of the commonly used gentiana (containing gentian; *Gentiana lutea*, Gentianaceae; *Long Dan Xie Gan Tang)*, Dr. Xie writes that it is "often used for the treatment of hepatitis, moist dermatitis, or otitis due to Liver Excess Heat in veterinary practice."

The third section of the text is described in the preface as "detailed information on how to apply Chinese herbal medicine in veterinary practice and how to select an herbal formula based on the TCVM pattern diagnosis." While it partially meets this description, details are lacking and many common conditions are not presented. It is the shortest section in the text and is the one that could most use development in future editions.

For example, a busy practitioner may wish to find a formula to treat diarrhea in the small animal. While several patterns can lead to diarrhea, a total of just 7 formulas are listed for diarrhea in the companion animal, yet there are many more formulas that could be listed here.

The author of this section also suggests specific products for each condition listed that can be purchased from a few of the many fine American producers of Chinese herbal formulas. Included most frequently are the products of the Jin Tang herb company, owned and operated by Dr. Xie. The selective reference to specific companies and products may be a turn-off to some veterinary herbalists, as this leaves an impression of favoritism and self-promotion that is usually not found in a textbook.

A bit of a self-serving purpose is also revealed in Appendix A, which chronicles the history of TCVM. Here, the Chi Institute (founded in 1998 and operated by Dr. Xie) is described as the leading school for TCVM continuing education programs, while the International Veterinary Acupuncture Society (IVAS), founded in 1974, is given only brief mention. IVAS, in fact, has trained over 5,000 veterinarians worldwide, and has been offering continuing education in veterinary acupuncture and herbal medicine since 1975. Courses have been held annually in the United States, and also have been taught in Canada, Australia, South America, and Europe. Modern-day TCVM in Japan and Europe is not even mentioned.

Overall, this text fulfills its purpose and will serve many veterinarians as a valuable resource. It is a respectable achievement on the part of Dr. Xie and the other authors and is certain to be found useful by students as well as practitioners. While there is room for more information in future editions, this text provides a solid foundation as the first of its kind to be published in the United States and will become a much-referenced text for years to come.

—Elizabeth Hassinger, DVM
Council of Elders, AHVMA
Wolf Rock Animal Health Center
Exeter, RI

The Chinese Medicinal Herb Farm: A Cultivator's Guide to Small-Scale Organic Herb Production by Peg Schafer. White River Junction, VT: Chelsea Green Publishing; 2011. ISBN: 978-1-60358-330-5. $34.95.

For gardeners, winter is a time to take stock of the previous year's successes and failures and to let the mind meander and plan for improvements and additions for the upcoming year. Peg Schafer's *The Chinese Medicinal Herb Farm: A Cultivator's Guide to Small-Scale Organic Herb Production*—based on her 15 years of commercial herb-cultivation experience—keeps my gardening spirit warm, but also fills me with new ideas and inspiration for farming Chinese medicinal herbs and plants of any heritage. Whether one is a novice to gardening or a seasoned farmer, this book is rich in advice and information pertinent to the ethical growing, harvesting, marketing, and conservation of medicinal plants.

"Chinese botanical medicine and other forms of botanical medicine are used by nearly one third of the world's population and continue to grow as a popular form of therapy," wrote Yung-chi Cheng, the chairman of the Consortium for Globalization of Chinese Medicine, on its website. Thousands of years of Traditional Chinese Medicine (TCM) practice are bound in empirical wisdom and have withstood the test of time and pressures from newer Western medical models. With the world's population soaring to more than 7 billion in 2011, there is a growing consumer demand for medicinal herbs. To meet expanding consumer needs, some herbs are grown in vast quantities with the use of pesticides and herbicides. Other herbs are wild-harvested, exploited, and threatened to extinction. Habitat-loss, due to development also puts pressure on sensitive plants to become at-risk or on the verge of being extirpated. Finding ecologically viable ways to cultivate herbs and retaining ancient growing traditions is the basis of Peg Schafer's work as a farmer, as a seller, and as a spokeswoman for domestically field-grown Chinese, Ayurvedic, and other Asian herbs in North America. She draws from her passion and her work to write this book.

This book is divided into 2 sections: Part One, "Cultivating to Conserve—Connecting with Quality Asian Botanicals" and Part Two, "Medicinal Herb Profiles." The first part of the book emphatically addresses issues of herbs grown according to Chinese tradition with a local, sustainable, and ecological mindset. When the source of herbs is far across the ocean, it is difficult to confirm the type of environment in which they were grown and harvested.

Folks want healing herbs, not ones grown with herbicides, pesticides, heavy metals, and other contaminants. Concerns about the methods by which the plants are grown and harvested abound. Are harvesters robbing the environment of endangered plants for economic gain?

A cultural and ecological cross-fertilization of East-meets-West—similar to the popular slogan, "Think Globally, Act Locally"—defines the book's farming philosophy of growing Asian plants in compatible North American ecosystems. A laudable goal of the book is to help growers across North America determine which Asian herbs grow best in their local regions. By growing the herbs in the United States—particularly for the US market—it is easier to ensure that the plants are cultivated and harvested in an organic, sustainable fashion. In addition, Schafer's book emphasizes cultivating plants that are not only of a high quality, but also of a wild quality. The objective is to cultivate wild-simulated crops. She convincingly points out that the wild-grown herbs, rather than "pampered," field-grown plants, have the potential to be more medicinal. She notes that "stresses from uneven water, nutrient availability, and insect and herbivore presence all elicit [mainly chemical] responses in the plants that amplify their medicinal value." Her book gives reliable information on how to farm with the intention of mimicking wild conditions and creating or utilizing microclimates that mirror native plant communities.

The first part of the book is suffused with discussions of polyculturally diverse intercropping (as opposed to monoculture farming), organic certification, Good Agricultural Practices (GAPs), genetically modified herbs (GMOs), regulations, and invasive and endangered species. With the push to bring jobs back to America, to reduce carbon consumption from excessive transport, and to better steward the land, it makes sense to educate and employ people to domestically grow their own organic medicinal herbs.

Schafer's years of farming experience are apparent in her beautifully written passages on planning, seeding, propagating, planting, weed management, harvesting, drying, storing, and marketing of Chinese herbs. She weaves her own tales of farming, laden with personal struggles and successes—giving the book a rich quality, as if she is speaking directly to the reader. In addition to the personal vignettes, I particularly like the easy-to-read tables that give regional adaptability, harvesting, and invasive information. There is much to glean by reading through this section. For instance, I did not know that coir, a planting medium made from coconut husks, should be "thoroughly leached, since most of it has a high salt content." The book gives step-by-step directions on how to leach coir; a recipe to make basic bark-based media mix; how to use a fan, large tarp, and ladder to clean seed; and the processing method for wet fruits from plants such as the traditional Ayurvedic ashwagandha (*Withania somnifera,* Solanaceae).

Globalization and immigration have brought plants from all regions of the world to North American soils. Some of these plants have prospered by virtue of similar ecosystems and lack of predators and have the capacity to spread rapidly and take over native woodlands as an ecological threat. In the woods near my home, Japanese honeysuckle (*Lonicera japonica*, Caprifoliaceae) and Oriental bittersweet (*Celastrus orbiculatus*, Celastraceae) vines strangle the native tulip poplars (*Liriodendron tulipifera*, Magnoliaceae) and maples (*Acer* spp., Sapindaceae), mile-a-minute (*Persicaria perfoliata*, Polygonaceae) annually smothers black walnut trees (*Juglans nigra,* Juglandaceae), silk trees (*Albizia julibrissin*, Fabaceae) readily naturalize in riparian areas, Japanese barberry (*Berberis thunbergii*, Berberidaceae) outcompetes native shrubs, and Japanese knotweed (*Polygonum cuspidatum*, Polygonaceae) forms dense thickets in wet areas.

Schafer addresses the invasive plant problem, and like her, I am concerned that people need to be informed and extremely responsible when planting some of the Asian medicinal plants that may spread beyond the boundary of where they were originally intended. The book has a section on managing invasive plant risk and a chart of potentially invasive Chinese herbs. Eventually, evolution will decide the fate of North America's native woods, and I suspect naturalization similar to that of the red fox, apples, horses, and dandelions (*Taraxacum officinale,* Asteraceae) will take place in hundreds or thousands of years. With time, it will be hard to separate native from non-native plants, but until then, growers and farmers of Asian herbs must keep an upper hand of what and where to cultivate these plants. I highly recommend reading through the book's section on weeds and invasive plants before deciding on species to grow in your region.

The second part of the book, "Herb Profiles," gives information on 79 "promising" medicinal herbs for domestic cultivation. The profiles include botanical nomenclature complete with synonyms, common names, Chinese Pinyin names, plant families, and the parts used. Also included are plant descriptions, cultivation and harvest techniques, companion planting ideas, field production, pest and diseases, and medicinal uses.

I am the garden director of Dr. Jim Duke's educational Green Farmacy Garden (GFG) in Maryland, where there are approximately 300 species of medicinal plants. According to the garden plant database, the GFG has 47 of the 79 herbs that Peg Schafer profiles. How I wish this book would have been available to me when I began my position at the garden! I would have greatly benefitted from the insight as to what to do with several of the Chinese medicinal plants that I had no prior experience with or had ever laid eyes on before. I learned that the unmanageable red, white, and green cultivar 'Chamelion' (*Houttuynia cordata,* Saururaceae; Pinyin: *yu xing cao*) "is considered less medicinally appropriate" than the dark green variety. Jim calls this plant "Hot Tuna" due to the homonym and also since its pinyin name means "fish-smelling herb." *Houttyunia cordata* sprouts prolifically from rootlets all over the garden's virus plot with overly optimum conditions of partial moist shade and is virtually impossible to maintain. Schafer indicates that to "curb its growth," one may want to withhold water, and I can guarantee that next summer, the irrigation will be turned off in the virus plot.

The garden also has a multitude of easy-to-germinate-and-grow *Angelica dahurica* (Apiaceae; Pinyin: *bai zhi*) to represent the difficult and "challenging to grow" *A. sinensis* (Apiaceae; Pinyin: *dang gui*). Here is an example of what Schafer emphasizes in seeking to find the appropriate ecosystem or microhabitat for a plant. Our garden has been unsuccessful in keeping dang gui alive year after year. Dang gui is indicated to reside in the hot, south-facing, Menopause plot, but it typically succumbs to the Maryland summers and is dead by August. Schafer suggests placing it in a "forested situation with deep, moist soil and duff cover" along with damp conditions from rain or irrigation. Her experience teaches me that "semiwild forest cultivation is superior to standard field production." Next year I will attempt to grow dang gui in the yin/yang valley—the north/south facing woodland adjacent to the garden.

The GFG is a seed bed for the invasive sweet Annie (*Artemisia annua*, Asteraceae; Pinyin: *qing hao*), and Jim likes to tell stories of his forays along the Shenandoah River and in China, finding this widely studied plant for malaria and cancer research. However, plant energetics, a very important aspect of TCM, never gets mentioned at our educational garden. For instance in the *A. annua* plant profile, Schafer writes that the "bitter, acrid and cold, *qing hao* clears heat and treats malaria, clears yin deficient heat, summer heat, and liver heat and cools the blood." This information may be irrelevant to a reductionist, Western-trained botanist like Jim Duke, but is very useful for a TCM practitioner or herbalist seeking the proper herb(s) in a holistic-energetic approach. In each herb profile there is a side note with information on the medicinal uses of the plant containing energetics, formulas, combinations of herbs, methods of administration, pharmacological implications, and modern research where applicable. Additionally, sprinkled throughout the second part of the book, one can find several tempting recipes such as licorice (*Glycyrrhiza* spp., Fabaceae)-flavored ginseng (*Panax ginseng*, Araliaceae) tea, Chinese rhubarb (*Rheum palmatum*, Polygonaceae) crumble, or loquat (*Eriobotrya japonica*, Rosaceaae) smoothie.

The book also contains several useful appendices. The first is a cross-referenced list of plant and medicinal names with 3 tables for the reader to cross-check botanical, common, and Pinyin names. The other appendices contain maps comparing the hardiness zones of China to the United States, maps and charts of climate zones and precipitation in China, useful resources of herb seeds and plants, conservation organizations, and recommended reading. Finally, there is a glossary of horticultural, medicinal, and pinyin terms. The medicinal terms are mainly related to Chinese or Ayurvedic medical systems and are not of the Western medical model.

The title of the first chapter, "Farming to Be Part of the Solution," resonates loudly with me as I suspect it will for most people who desire to grow their own high-quality Chinese herbs. The impetus to farm in the ecological fashion presented in the *Chinese Medicinal Herb Farm* makes me want to jump out of my comfy chair on this winter day, get my hands dirty, and start making to-do lists of seeds to buy and projects to take on. However, with the dismal weather outside, I will happily settle for Peg Schafer's recipe for sweet vine tea from the *Gynostemma pentaphyllum* (Curcurbitaceae; Pinyin: *jiao gu lan*—the only plant containing ginsenosides outside the genus *Panax*) I organically grew and sustainably harvested this past summer.

–Helen Lowe Metzman
Garden Director
Jim Duke's Green Farmacy Garden
Fulton, MD

Mycophilia: Revelations from the Weird World of Mushrooms by Eugenia Bone. Emmaus, PA: Rodale Books; 2011. Hardcover; 368 pages. ISBN: 978-1605294070. $25.99.

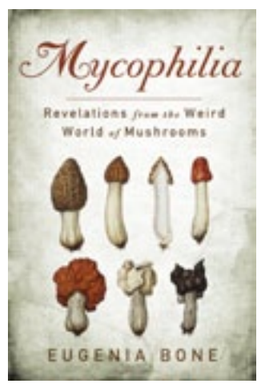
Mycophilia is in essence a very personal and colorful topical travel guide. It is written in an informal, conversational style, laced generously with personal anecdotes and opinions of the author, as well as thoughts about experiences she had during fungi forays, conferences, and interviews. What came to mind after reading through the book was a subtitle for it: "A Field Guide to the Wacky World of Mushroom Nerds and the Fungi They Love."

The book is divided into 12 chapters, starting with details of the author's travels through the world of mycologists and mycological conferences. These gatherings are not research-focused, droll, and erudite meetings reporting on the latest taxonomy based on alignment of DNA sequences, but rather colorful and eclectic gatherings of mushroom lovers. Her book is bountifully laced with stories and quotes from figures of note such as University of Wisconsin-La Crosse biologist, Tom Volk; pre-eminent fungophile Paul Stamets of Fungi Perfecti; and Gary Lincoff of the New York Botanical Garden.

The author forays into the world of mushrooms and describes them as important components of the forest ecology, as well as what they eat, who eats them; and their microscopic interactions with other organisms, such as the mycorrhizal associations with trees and many other plants. The topic of mycorrhizal interactions and fungal endophytes living between the cells of plant leaves is a highly active and fascinating area of scientific research, and Bone introduces the reader to these topics with flair.

Throughout the book, the author documents and tells tall tales about people who collect mushrooms for a living on the "mushroom trail." These individuals live below the radar in the woods and travel extensively collecting "non-timber forest products" in the Western US and other far-flung places. It is an interesting social phenomenon based on a seasonal nomadic lifestyle.

Further chapters explore mushroom cultivation, including the author's personal experience with kitchen-counter cultivation, the allure and excitement of morel hunting, truffle hunting and eating, truffle products and marketing, and more information than one could hope for on the world of button mushrooms, *Agaricus bisporus* (Agaricaceae)—the world's most cultivated fungus—as well as the straw



mushroom and others. In later chapters, Bone writes about the nutritional and medicinal value of mushrooms in the diet and as nutraceutical products, again interspersed with personal stories offered as an unabashed "mushroom groupie." She reports on the healing properties of mushrooms, including the cultural uses of mushrooms as medicine, with a brief review of some of the latest scientific research, focusing on some of the major species such as shiitake (*Lentinula edodes*, Marasmiaceae), reishi (*Ganoderma lucidum*, Ganodermataceae), and cordyceps (*Cordyceps* spp., Clavicipitaceae). As is the nature of this book, the practical details are blended with stories about the history, people, and places from which, whom, and where the practical uses of fungi are taught.

A book about the world of mushroom lovers would hardly be complete without some discussion of fungi as mind-altering substances, *e.g.,* psylocybin mushrooms (*Psilocybe* spp., Strophariaceae), mushrooms in shamanistic practice (*Amanita muscaria*, Amanitaceae), and their use in popular Western cultures today. Bone does not neglect this popular topic, devoting a chapter titled "Shrooms" to a narrative on some of the history, lore, and modern research on the benefits and potential dangers of hallucinogenic fungi. Psilocybin mushrooms were outlawed for legitimate scientific study until only recently, but new research now shows that ingesting them can make positive and lasting changes to one's personality, engendering a positive and more philosophical outlook on life. She closes the book with a look at mushrooms for bioremediation of toxic sites, as a producer of biofuels, and other useful technologies—an area pioneered by Stamets *et al*.

Mycophilia doesn't include recipes for those interested in fungi from a culinary standpoint, and it isn't a reference guide to help one identify various useful fungi. The book does not provide practical details about how to prepare mushrooms for medicine, for instance how to make tinctures, teas, or other extracts. Neither does it take much of an in-depth view of the biology or systematics of the Kingdom Fungi. Some details about mushroom biology and the uses of mushrooms are woven throughout the text, but retrieving specific information is difficult, because the book is not ordered or referenced in such a way that would facilitate its easy access. Many of the references given in the extensive "Notes" section for each chapter are secondary or even tertiary sources—books and magazine articles that draw from either the primary or secondary literature. The author also includes references to conversations she recorded from mushroom researchers and "mushroom heads." To her credit, Bone does cite some relevant primary literature, though these articles are not always easy to connect with particular statements in the text.

Mycophilia is not a reference guide to access practical information about how to use fungi as food or medicine. It is a great book to take with you on a vacation or to a hot springs (where I am writing this). Full of colorful stories of colorful people who have helped bring the idea of beneficial fungi to a broader popular audience, it makes a relaxing and interesting read, especially if you like a warm, conversational, and personal style.

–Christopher Hobbs
Doctoral Candidate, Department of Integrative Biology
University of California, Berkeley

Teas, Cocoa and Coffee: Plant Secondary Metabolites and Health by Alan Crozier, Hiroshi Ashihara, and Francisco Tomas-Barberan (eds). West Sussex, UK: Wiley-Blackwell; 2012. Hardcover; 252 pages. ISBN: 978-1-4443-3441-8. $144.99.

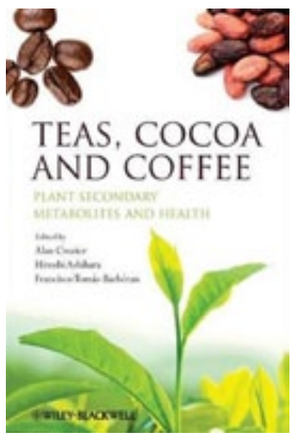
This excellent text on the health benefits of 3 widely popular foods—tea-, coffee-, and cocoa-derived natural products—covers a range of current topics of interest and focuses on the properties of the plants' dominant components including purines (primarily caffeine, theobromine, and theophylline), phenolic acids, and flavanols/polyphenols. The book also provides comprehensive background information on bioavailability and the effects of these classes of phytochemicals on human health. Secondary metabolites, as these chemicals are known, are not essential for the existence of the individual or species, but often play a key role in its successful survival over others.

Teas, Cocoa and Coffee consists of 8 chapters written by 16 prominent researchers from 4 countries and includes discussions of the origins and history of each of the 3 ingredients. Additional chapters examine the chemical constituents of each of these popular plants and include wide-ranging details on their bioavailability and thorough coverage of human health effects.

As an example, Chapter 6, "Coffee and Health," summarizes hundreds of epidemiological studies on coffee consumption and its beneficial effects on type 2 diabetes, heart disease, and various cancers. The chapter also includes a discussion of inflammation effects and the antioxidant statuses of certain components of coffee.

Another fine example of the book's detailed coverage is Chapter 4,"Teas, Tisanes and Health," which summarizes the published clinical trials of various commercialized teas (*Camellia sinensis*, Theaceae), including black, green, and oolong, plus the popular herbal teas yerba maté (*Ilex paraguariensis,* Aquifoliaceae), chamomile (*Matricaria recutita*, Asteraceae), hibiscus (*Hibiscus* spp., Malvaceae), and rooibos (*Aspalathus linearis*, Fabaceae). The clinical data on *C. sinensis* consumption and observed beneficial effects on cardiovascular health are compelling.

These fields of preclinical and clinical research are advancing rapidly, and the materials covered by this text provide a comprehensive profile of the health effects of these 3 plants. This book should be considered for inclusion in the library of all researchers with



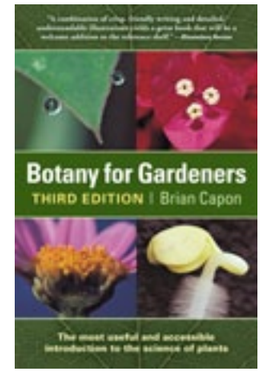
an interest in natural products chemistry in general, as well as those with an interest in biochemistry, nutrition, or food science. For researchers with a particular interest in the phytochemistry, biochemistry, human health applications, nutrition, or bioavailability/absorption of teas, cocoa, or coffee, this monograph is a required desk reference. Additionally, this text should be included in all college and university science and medical libraries, as there are no comparable up-to-date treatises on the health benefits, composition, and bioavailability of teas, coffee, and cocoa.

–Michael S. Tempesta, PhD
Managing Partner
Phenolics, LLC
El Granada, CA

Botany for Gardeners, 3rd Edition by Brian Capon. Portland, OR: Timber Press; 2010. Paperback; 268 pages. ISBN 978-1-60469-095-8. $19.95

All life depends on plants—they are amazing, and understanding how they grow, reproduce, and respond to a range of factors is an essential part of knowing how to work with and appreciate them. *Botany for Gardeners* is not only a reference book, but a great read as well. The book provides a way to refresh one's knowledge of how plants work even as it maintains an interesting, current, and comprehensible tone. It is not a how-to book; rather, it is a book about understanding the complexities of plants and why they do what they do. The third edition is essential as it keeps pace with our knowledge of the new discoveries and research on plants.

The English-born author, Brian Capon, PhD, a retired professor of botany at California State University, compiled this book based on lecture notes he used to teach botany for non-science students. Not only is the text engaging, the illustrations and photographs help clarify and visualize the descriptions. The book begins with explanations of plant growth, cells and seeds, roots and shoots, followed by travels inside plant stems, roots, and leaves. Next is an exciting focus on plant adaptation—an area of amazing revelations and survival techniques—then an overview of plant functions such as growth, development, uptake of water, minerals, and light. In the final sections, the focus is on flowers, pollination, reproduction, and strategies of inheritance, all filled with fun facts about plants while providing clear descriptions.



Botany for Gardeners opens with detailed accounts of the structure and function of plant cells, featuring outstanding drawings and photographs that help distinguish cell structures and demonstrate the processes of cell division. The description of seed germination that follows will help any gardener trying to understand seeds' behavior, needs, and responses to a variety of settings.

Much of the book gives the reader a sense of actually *getting inside* a plant. The author clarifies how water and minerals move through the plant and how roots, stems, and leaves operate. For example, the author explains the concept and power of transpirational pull—the process of water's entering the roots, moving through the plant's interconnecting xylem, and up through and out of the leaves in the form of transpired water vapor—with enjoyable crispness.

It is thrilling when a book captures the excitement of photosynthesis. In the process of photosynthesis, plants absorb light and transform it into food. Plants can be considered large-scale storers of sunlight in the form of energy-rich food molecules and are the intermediaries between the sun and all other creatures on earth. This knowledge reinforces our appreciation for the critical importance of plants to humans and the environment.

Appropriately, there is extensive information on plant adaptation. Since plants can't move like animals, they have developed some extraordinary abilities to attract pollinators, to defend against attackers, and to survive in extreme environments. Plants send signals and have complex relationships. The bullhorn acacia (*Acacia sphaerocephala*, Fabaceae) is a great example of a complex symbiotic relationship. The plant produces a nutritious liquid from specialized glands that attracts ants. Ants live inside the large thorns of the acacia so that if the plant is disturbed, the ants rush out in a frenzy, thereby protecting the plant from attack by other insects.

From the intrigue of roots and mycorrhizae to the steps from flower to fruit and plant genetics, the complexities of plants are made clear and brought to life in this text. Additionally, brief sections throughout the book on topics such as plants as food, implications of global warming, genetic engineering, and electron micrography of pollen grains and diatoms—which reveal the exquisite hidden beauty of plants—are welcomed additions.

Written by a plant lover, *Botany for Gardeners* creates a sense of awe about plants and provides accessible language, photographs, and drawings describing the mechanics and the magic of plants. This book should stay close by as a handy reference as well as a friendly guide to both the botany and physiology of plants.

–Holly H. Shimizu
Executive Director
US Botanic Garden

The Tea Horse Road: China's Ancient Trade Road to Tibet by Selena Ahmed and Michael Freeman. Bangkok, Thailand: River Books Co. Ltd.; 2011. Hardcover; 340 pages. ISBN: 978-9749863930. $65.00. Available in ABC's online store. (Catalog # B585)

BOOK REVIEWS

"*Tea Horse Road* is a narrative of politics, economy, culture, and health. It is about ascending empire, a desire for the exotic, and a more humble quest for energy, well-being, and livelihood."

So begins the tale of this book. As the book explores an extensive network of physical pathways and small local routes that came to be collectively known as the Tea Horse Road. For centuries, this road carried tea out of the forests of Yunnan Province, China, south to Tibet, Nepal, India, and Burma.

An astonishing feat abounding with staggering perils and danger, the Tea Horse Road was so important that a former trade route—the Southwest Silk Road (*Xi'nan Sichouzhilu*), which connected China with neighboring countries (and along which goods such as silk, jade, wool, furs, salt, and silver were transported from east to west and back again)—was renamed the Tea Horse Road (*Chama Dao*) after tea became the most sought-after commodity that traveled the route.

Beginning in the 7th century, the Tea Horse Road transported tea over the Himalayas by caravans of men and mules. This road served this essential duty until the mid-20th century when paved, motorized highways made the transport of tea faster and easier and rendered the perilous old routes obsolete.

This book is imposing in size (340 pages) and considerably heavy. At first glance it appears as though it might be just another pretty coffee-table picture book. Indeed, Michael Freeman's wonderful black-and-white photographs appear throughout and offer stark contrast to vivid color images of the rugged landscape and hearty people who live in this area of China and Tibet.

But readers who sit and linger with this book will find that it contains riches. Well-written, concise text effectively introduces the reader to this colorful part of the world and the importance that both the Tea Horse Road and tea have had to the people who have populated this region for generations.

Yunnan Province has a wealth of natural resources, a grand history, unique cultures, and one of China's most treasured teas. For me, what sets this book apart from other books I have read on the topic of the Tea Horse Road is the author's use of the present to help understand the past. In the spirit of the meandering local side paths of the Tea Horse Road that brought traders and tea to small pockets of local populations, the author, too, brings the reader along divergent paths and into the lives and cultures of people in Yunnan, Sichuan, Tibet, Burma, and India who were and still are affected by the Tea Horse Road.

I like the layout of the book and the chapter designations. The story moves from place to place, adding bits of relevant information, rather than just following a historical timeline. And I am especially pleased to see the full-sized map positioned in the early pages that clearly illustrates the routes of the Tea Horse Road. I think that maps are essential, and I appreciate editors and publishers who understand how helpful maps are to readers.

Selena Ahmed, co-author with photographer Michael Freeman, is an ethnobotanist who has conducted research in Yunnan for years. Her particular interest is in the villages of Yunnan and the tea production systems in place there.

As such, she understands that the Tea Horse Road did not exist in isolation from its surroundings and that its location was not happenstance, but that it developed because of many factors particular to Yunnan. By taking a long and wide look at the history and culture of this place, she breathes life into her narrative by discussing much more than just the history of the tea road itself.

For instance, we learn about the tea that traveled over the Tea Horse Road—what we call *pu-erh* today. Since earliest recorded time, tea has been made in Southwest China with leaves plucked from large leaf varieties of tea bushes or trees *(Camellia sinensis*, Theaceae). From those early days until now, tea has evolved from a crude, simple food to a medicine, a tonic, and ultimately to a pleasurable beverage. Tea underwent profound changes brought about by dramatic weather as it moved along the Tea Horse Road, and those changes most certainly influenced how the tea was processed after that fact became known.

Readers learn the story of pu-erh and why its importance to the people of this region continues today. The best pu-erh is still made using traditional processes and by following certain criteria in leaf plucking and tea manufacturing and

New Book Profiles

The Healing Plants Bible: The Definitive Guide to Herbs, Trees, and Flowers by Helen Farmer-Knowles. New York, NY: Sterling Publishing; 2010. Paperback, 400 pages. ISBN: 978-1-4027-7551-2. $14.95.

The Healing Plants Bible is a pocket-sized guide to common medicinal plants. In her brief introductory section, Helen Farmer-Knowles writes that the book "is not intended as a guide to prescribing herbal treatment or for curing ailments and disease. It is meant as an inspirational reference source to help you learn more about … phytotherapy." The plants in this small, full-color guide are organized into 5 sections: "Healing and Medicinal Herbs," "Edible Healing Plants," "Healing Energies of Trees," "Plants for Spiritual Healing," and "Flower Essences."

Field Guide to Wildflowers of North America by David M. Brandenburg. Foreword by Craig Tufts. New York, NY: Sterling Publishing; 2010. Paperback, 674 pages. ISBN: 978-1-4027-4154-8. $19.95.

The National Wildlife Foundation's *Wildflowers of North America* is a comprehensive and easy-to-navigate guide that is as attractive as it is useful. The colorful book is smartly organized by plant family and features a waterproof cover for outdoor use in inclement weather. The introduction comprises a color-based identification aid and a primer on plant structure and wildflower conservation efforts. Each plant family is further divided into sections by genus. The most common wildflowers in each genus are featured, and each section contains photographs and a geographic distribution map.

Practical Herbs by Henriette Kress. Helsinki, Finland: Yrtit ja yrttiterapia Henriette Kress; 2011. Paperback, 150 pages. ISBN: 978-952f-67575-0-6. $32.00.

Practical Herbs is Finnish herbalist Henriette Kress's first English-language book. Well-known on the internet for her highly robust website, "Henriette's Herbal," she covers the basics of making herbal teas, oils, tinctures, and salves using self-harvested plants. Although the 23 herbs elaborated upon in this book are most commonly found in Finland and Northern Europe, this guide would be useful for anyone living in a temperate climate. Each section contains information about the plant's habitat, appearance, and similar-looking herbs, as well as details on picking, processing, and the herb's intended effect. Recipe ideas and potential adverse side effects are also included.

Traditional Chinese Medicine Approaches to Cancer: Harmony in the Face of the Tiger by Henry McGrath. Philadelphia, PA: Singing Dragon; 2009. Paperback, 254 pages. ISBN: 978-1-84819-013-9. $18.95.

In *Traditional Chinese Medicine Approaches to Cancer*, Chinese medicine expert Henry McGrath presents alternative treatments for various types of cancer. According to the author, these treatments are not meant to replace a Western medicine approach, but are useful as part of an integrative, complementary approach for symptom management and as a preventative measure. He argues that a Chinese approach to medicine takes the entire person into consideration—including the mind—while Western medicine tends to focus solely on the disease and its symptoms. The book includes a basic introduction to Chinese medicine and McGrath discusses acupuncture, herbal medicine, and nutrition in great detail.

Celestial Healing: Energy, Mind and Spirit in Traditional Medicines of China, and East and Southeast Asia by Marc Micozzi. Philadelphia, PA: Singing Dragon; 2011. Hardcover, 222 pages. ISBN: 978-1-84819-060-3. $24.95.

In *Celestial Healing*, author Marc Micozzi MD, PhD, discusses the ethnomedicine traditions of eastern Asia. Each chapter is organized into a section based on geographic area. These sections include Part 1, "China," Part 2, "East Asia," Part 3, "Southeast Asia," and Part 4, "Chinese Medicine in the West and Worldwide." Despite the differences in these related systems of healing, Micozzi, who has both a medical and an anthropology doctorate, says that there are 2 concepts common to each system: "(1) the *celestial origins* of medical knowledge and healing practices, and (2) the key to all life, health, and healing is *vital energy* that influences all aspects of medical practice."

Vital Healing: Energy, Mind and Spirit in Traditional Medicines of India, Tibet and the Middle East – Middle Asia by Marc Micozzi. Philadelphia, PA: Singing Dragon; 2011. Hardcover, 231 pages. ISBN: 978-1-84819-045-0. $24.95.

In *Vital Healing*, Marc Micozzi, MD, PhD delves into the ethnomedicine traditions of the Middle East and Middle Asia. As in his related book, *Celestial Healing*, the author examines the influence of Chinese medicine on medical traditions in different regions of Asia. "The healing traditions we encounter in this book consider spiritual consciousness to be of primary importance in maintaining optimal health, emphasizing meditation and movement practices and other modalities that foster integrated (holistic) functioning of the nervous system," he writes.

Alzheimer's Disease: What if There Was a Cure? by Mary T. Newport. Laguna Beach, CA: Basic Health Publications, Inc.; 2011. Paperback, 398 pages. ISBN: 978-1-59120-293-6. $18.95.

Mary T. Newport provides a personal account of her struggle caring for her husband with early-onset Alzheimer's disease and offers details of an emerging treatment for the disease using ketones—a group of organic compounds. Ketones are created when fatty acids undergo a series of reactions in the liver. Ketones can then be used as an energy source in cell mitochondria—the "power plants" of cells—including the mitochondria in the brain. Newport recommends consuming medium-chain fatty acids, such as those found in the increasingly popular coconut and palm kernel oils, which are converted to ketones.

Our Toxic Legacy: How Lead, Mercury, Arsenic, and Cadmium Harm Our Health by Beatrice Trum Hunter. Laguna Beach, CA: Basic Health Publications, Inc.; 2011. Paperback, 327 pages. ISBN: 978-1-59120-284-4. $19.95.

In *Our Toxic Legacy*, author Beatrice Trum Hunter presents evidence for the toxicity of 4 metals: lead, mercury, arsenic, and cadmium. She argues that the government has taken minimal, reactive measures to incidents involving these metals, as opposed to taking proactive measures to prevent harm. The book is divided into 4 chapters: Chapter 1, "Lead: The Cause of a Vast and Silent Epidemic," which comprises roughly half of the book's content; Chapter 2, "Mercury: Destroyer of Body and Mind;" Chapter 3, "Arsenic: A Jekyll and Hyde Metal;" and Chapter 4, "Cadmium: A Biologically Non-Essential, Non-Beneficial Human Toxin."

Wan's Clinical Application of Chinese Medicine: Scientific Practice of Diagnosis, Treatment and Therapeutic Monitoring by Giorgio Repeti. Philadephia, PA: Singing Dragon; 2011. Paperback, 160 pages. ISBN: 978-1-84819-047-4. $29.95.

In *Wan's Clinical Application of Chinese Medicine*, author Giorgio Repeti shares the teachings of his mentor and well-known Chinese medicine doctor Master Wan. The book focuses on a particular system of Chinese medicine known as the 3E approach. Practitioners using the 3E approach look to treatment options that are *efficient, easy, and economical*. Chapters include "Wan's 3E Diagnostic Method," "Radial Pulse," "3E Acupressure," "3E Acupuncture: The Essentials," and "3E Herbal Medicine: Cold and Hot Syndromes."

storage of the tea after production.

Yunnan's teas (there are green and black teas, in addition to pu-erh) are unique because of many variables: *terroir* (place) of the region, which includes climate, geography, soil conditions, humidity, and rain patterns, and also because the Mekong River has played a pivotal role in keeping this area vital. Over time, many cultural groups have navigated along this waterway mingling tea seeds and tea culture with them as they traveled from the old homelands to new ones in both upland and lowland areas.

Many of these ethnic groups (Akha, Dai, Hani, Jinuo, and others) trace their roots to ancestors who have lived in these forests for centuries. The 12 Tea Producing Mountains (a reference to the most famous tea growing mountains where many of these ethnic groups live) still maintain old-growth tea tree forests (multi-generational descendants of wild-growing, indigenous tea trees). This is in contrast to the large tea factories and cultivated tea gardens (once operated by the Chinese government in the 20th century but now privately owned) that are located further down the mountains near the cities.

For some of these people and their villages, the old tea trees are their patrimony and their children's inheritance. These trees are a link to their ancestors who took care of the tea trees and made distinctive tea of their own cultural preference from these large-sized tea leaves. This region claims the oldest association between humans and the tea bush. Ancestors of these ethnic groups grew and nurtured ancient tea trees and consumed tea before China existed as a unified state.

The biodiversity in Yunnan's tea forests stands in opposition to the intensive mono-cultural practices of modern tea farming. The message here is that much can be learned from the tea farmers in the old-growth tea forests, and that intensive tea-growing practices, in its haste to bring more product to market faster, can lead to the destruction of land, genetically diverse plants, and in some cases, cultural practices.

The author introduces the reader to some of the mountain- and hill-dwelling ethnic people who populate this region; compelling photographs bring the reader into their lives, creating the feeling that we are experiencing a small measure of their culture and the hardships they face living in these stunning but remote places. These are the faces of many of the people who make these incredible teas by following traditional, learned practices.

In addition to the story of the tea, *Tea Horse Road* is the story of the men (muleteers) and their mules that traveled long and perilous journeys from Yunnan and Sichuan over dangerous roads in hostile weather conditions with their precious cargoes of tea bound for Tibet, Nepal, and later, India and Burma. It took many months for the caravans to make a round-trip journey, laden with goods for Tibet one way and goods bound for China on the return journey.

As the author writes: "the task was strenuous and the terrain unforgiving." The stories of these journeys defy belief, yet some of these men are still alive to tell them. Michael Freeman's photographs of some of the few men still alive from those days and the terrain over which they traveled give proof to wary disbelievers.

By the end of this book, readers have been treated to a story with many intertwined and nuanced layers and one that has elements worthy of an epic novel: an astonishing commodity, stunning and dramatic geographic locations, rugged people, and traditional ways of life and cultures that survive today.

I have traveled in Yunnan Province learning about tea, and I am still in awe of everything about this province. From the link between the tea and the tea plants, the plants to the environment, the environment to the ways of the people, and the people to their culture, religions, and their tea-drinking habits, I can say honestly that there is no other tea place in China quite like it. Reading this book and luxuriating in the photographs brought me back to tea-producing villages in Yunnan Province that I have visited. I am inspired to return and to learn even more about this epic chapter of tea culture.

–Mary Lou Heiss
Co-owner, Tea Trekker
Co-author, *The Story of Tea*, *The Tea Enthusiast's Handbook*

Finn Sandberg 1920–2011

Internationally respected pharmacognosist and medicinal plant researcher Finn Sandberg, PhD, passed away in July of 2011 at 91 years of age. Among his many accomplishments, he is remembered as one of the pioneers of the Asian Symposium of Medicinal Plant Science, Spices and Other Natural Products (ASOMPS) conference series and a champion for scientists in developing countries.

Professor Sandberg "was a man with many facets: pharmacologist, pharmacognosist, phytochemist, herbal products enthusiast, etc.," said R.O.B. Wijesekera, a former colleague who memorialized Prof. Sandberg in an article in *Link Natural Products Digest*—the newsletter of the Sri Lanka-based company Link Natural Products, which specializes in Ayurvedic health, wellness, and personal care products.[1,2]

"There was no question regarding his dedication and genuineness," said Wijesekera (email, March 16, 2012). "Personally, I shall miss his cheery presence as will so many scientists the world over."

In his early career, Sandberg joined the Royal Institute of Pharmacy in Stockholm, Sweden in 1954, as a professor of pharmacognosy.

"He was very much respected in the beginning of his career," said Lars Bohlin, PhD, a former student and colleague of Prof. Sandberg's (email, February 17, 2012). "He introduced both pharmacology and biochemistry as new subjects in the curriculum, [and] he developed pharmacognosy from morphology to a modern subject including phytochemistry and pharmacology."

At times, Sandberg's research focused on the pharmacological properties of plant alkaloids and saponins, both of which are naturally occurring secondary metabolites. Later, he became interested in medicinal plants on a global scale.

Sandberg was also known for having developed a simple field test for detecting biological activity in plant extracts. "He delighted in demonstrating this technique in workshops held in several developing countries, including Indonesia and Ghana," said Jack Cannon, a friend and former colleague of Prof. Sandberg's (email, March 19-28, 2012).

In 1968, Sandberg transferred to Uppsala University, where he spent most of his professional life. In addition to his reputation as a researcher, Sandberg was instrumental in creating a series of medicinal plant conferences in in Asia.

"[Finn] took a leading role in the establishment of ASOMPS, which … soon became a major forum for young scientists in Asia," said Cannon. "In later years, scientists from industrialized countries were attracted to these meetings, and the research of scientists in the region reached a wider audience."

Cannon is currently working on a history of ASOMPS, which he says is a tribute to Prof. Sandberg's vision and accomplishments. "It was planned to present a specially bound copy of the history to Finn at ASOMPS XIV," said Cannon. "However, Finn's illness and the unrest in Pakistan forced the indefinite postponement of ASOMPS XIV, and the history … remains unpublished."

Shortly after his 80th birthday, Sandberg co-authored *Natural Remedies: Their Origins and Uses* (Taylor & Francis, 2001) with Desmond Corrigan of Trinity College in Ireland. The 192-page pharmacognosy textbook, designed for pharmacy students and others, begins with an introduction to the history of botanical pharmacognosy and quality control of herbal medicines. The largest section of the book, organized by body system, contains descriptions of herbs used for various ailments.

Later in his career, Sandberg traveled extensively throughout Africa, South America, and Asia on research expeditions. Wijesekera described him as "a man who developed a tenacious rapport with the scientific researchers of four continents."[1]

"[One of] his most proud achievements was that he inspired research in so many laboratories around the world doing hands on duty in conditions so different from his native Sweden," said Wijesekera. "Many of the third world scientists he associated with became his lifelong colleagues and some of the younger ones even became his students."[1]

In recent years, the ASOMPS committee proposed the creation of the Sandberg Medal for research in plant-based bioactive agents by scientists in developing countries. "It is an objective we sincerely commend to a sponsor as a fully worthy one," said Wijesekera. "With him now gone the scientists of the third world and those dedicated to phytochemistry, pharmacology, and bioactive plant products, have lost perhaps their best friend."[1] HG

—Tyler Smith

References

1. Wijesekera R. A memorial tribute to a global authority on medicinal plants. *Link Natural Products Digest.* 2011; 7(2):27.
2. Welcome to Link Natural Products. Link Natural Products website. Available at: www.linknaturalproducts.com. Accessed March 28, 2012.

As all plants are made resplendent by sunshine and dew,
Our world is made richer by the life of one like you;
If you seek Finn's monument, then look around the world,
For the tradition of his learning his wisdom and his name;
But surely he lived for ends, more durable than fame.[1]
R.O.B. Wijesekera

May 22-24: Vitafoods Europe. Geneva, Switzerland. Part trade show and part conference, this event brings together more than 500 companies and leading experts in the dietary supplements, functional foods, and nutraceutical industries. In addition to numerous exhibitors showcasing their newest and most popular products, Vitafoods also offers poster sessions, a pavilion highlighting service and equipment providers, and a seminar theater where exhibitors discuss research and development activities. The conference portion of the event will feature keynotes on the history of the nutraceuticals industry and structures of the medical healthcare system, as well as sessions on consumer insights and the latest trends, preventative health and immunity, ageing consumers, digestive health, bone and joint health, brain and mind health, and food allergies. More information is available at www.vitafoods.eu.com.

May 24-25: Stevia Tasteful 2012, Food & Beverages Formulation -- The Subtle Balance. Paris, France. Sponsored by the World Stevia Organization (WSO), this event takes a new focus by discussing only food and beverages formulated with the naturally sweet herb stevia. According to the WSO, one central question remained after last year's conference on all things stevia—"how to limit and hide the aftertaste of Stevia in food and beverages?" So, the entire 2012 conference will feature discussions from research and industry experts on how to "reach the perfect balance" in products formulated with stevia. The event's objectives are to highlight recent advances in science, the latest regulatory policies, marketing tools, and strategies successfully employed by various companies, as well as how formulation can affect stevia taste and aftertaste. More information is available at www.wso-site.com.

May 26-27: Planting the Future. Williams, OR. Sponsored by the nonprofit United Plant Savers and the herbal product manufacturer Herb Pharm, this event aims to be "a medicinal plants gathering for herb enthusiasts of all levels." Held at Herb Pharm's 85-acre organic herb farm, attendees will enjoy sessions on comfrey, herbs for women, growing medicinal herbs in a backyard garden, medicinal aquatic plants, ethical wildcrafting, essential oils, and the endocannabinoid system. Expert speakers include Amanda McQuade Crawford, Kevin Spelman, Jonathan Treasure, and more. Herb Pharm co-founder Ed Smith will present "The Botanical Adventures of Herbal Ed," Mark Disharoon will lead a Wild Weeds Walk, and Jane Bothwell will lead an herb walk in Herb Pharm's impressive display garden. More information is available at www.herb-pharm.com/PTF_2012.

June 2-4: Medicines from the Earth Herb Symposium. Black Mountain, NC. This year's symposium will kick off with 3 unique pre-conference intensives on the effect that stress can have on digestive health, ethnobotany of native plants, and medicinal culinary herbs, vegetables, and fruit. The opening keynote address—discussing 21st century herbalism and full spectrum herbal medicines and phytomedicines—will be led by Mary Bove ND, Chanchal Cabrera, and Jill Stansbury, ND. Additional session topics include herbal therapeutics, herbal first aid, environmental illness, organic herb cultivation, and little-known indigenous plant medicines. Attendees can also participate in herb walks, the "Green Temple of the Holy Clovers," and an exhibit hall. More information is available at www.botanicalmedicine.org/conferences/me2012/me2012genl.htm.

July 9-11: The 16th International Congress PHYTOPHARM 2012. St. Petersburg, Russia. This year's event covers the scientific aspects of the pharmaceutical industry, with a special focus on new technologies in the development and pharmacology of natural medicines. Plenary lectures and discussion sessions will address the topics of nutraceuticals and medicinal plant products, medicinal plant ecology, quality control of herbal products through phytotechnology, pharmacology and ethnopharmacology, and the EU regulation of herbal medicinal products and food supplements. More information is available at www.ipharm.sp.ru/Phyto12/Introduction.html.

July 28 - August 1: International Congress on Natural Products Research (ICNPR). New York, NY. Sponsored by the American Society of Pharmacognosy and several European pharmacognosy societies, this event consists of symposia and oral sessions focused on global change, natural products, and human health. Attendees will have the opportunity to listen to numerous featured speakers—such as Prof. Doug Kinghorn, Prof. Harry Fong, and Steven King, PhD—who will discuss topics ranging from biodiversity and ethnobotanical drug discovery to genome mining and advances in biosynthesis. There will also be a symposium dedicated to the 75th volume of The J*ournal of Natural Products*. The event ends on Sunday evening with a social event at the New York Botanical Gardens. More information is available at www.icnpr2012.org.

September 6-15: IUCN World Conservation Congress. Jeju, Korea. Held every 4 years, the Congress for the International Union for the Conservation of Nature (IUCN) is an open forum to discuss major concerns and solutions relating to sustainable development. IUCN is a democratic, member-based organization that has been working to conserve the diversity of nature since 1948. This congress has the theme of "Nature+", which, according to IUCN, is a slogan that "captures the fundamental importance of nature and its inherent link to every aspect of our lives." Topics of focus will be climate change, food security, social and economic development, governance, and conservation. More information is available at www.iucnworldconservationcongress.org.

More calendar listings at
www.HerbalGram.org
See "News" Tab

In this department of *HerbalGram*, we list resources such as publications, organizations, seminars, and networking opportunities for our readers. A listing in this section does not constitute any endorsement or approval by *HerbalGram*, ABC, or its Advisory Board.

SupplySide R&D Insights, a new website from VIRGO Publishing, focuses on the research and development (R&D) side of the herbal and dietary supplements community. The online resource's content is totally focused on science and research conducted to back up health claims, and aims to inform and guide buyers in acquiring "trusted ingredients," which Virgo CEO John Siefert said is "the biggest issue facing finished product manufacturers." Available free-of-charge to website visitors are focus reports, which feature industry experts' advice on working with ingredient suppliers that have strong R&D portfolios; case studies on successful products based on strong R&D programs; slide shows, webinars, whitepapers on leading companies' experiences and best practices; digital issues of the new publication *R & D Insights Magazine*; and weekly columns. Sponsored by Indena. Available at: http://rd.supplysideinsights.com/.

Leanwashing Index rates the accuracy, adequacy, and transparency of food and beverage-related health claims and advertisements from companies, organizations, and individuals. Available online, the Leanwashing Index is a sister site to the Greenwashing Index, which assesses numerous environmental-related claims. According to the website, "'leanwashing' occurs when a company exaggerates or misleads consumers about health benefits through advertising, marketing, or packaging." Both indices are based on a rating system developed by University of Oregon School of Journalism and Communication professors, and modified and overseen by an advisory panel. The Leanwashing Index rating scale ranges from 1 to 5, with 1 being "authentic" and 5 being "bogus." All users are free to post and rate ads and claims, resulting in a broad mixture of experiences and responses. Ads are then arranged and showcased according to their average rating. Available at: www.leanwashingindex.com.

The US Pharmacopeial Convention (USP) recently launched its new website. The updated and redesigned online resource presents USP's wealth of scientific information in a simple and easy-to-navigate format. Content is now organized by subject through 8 user-friendly tabs at the top of the page — including a tab for dietary supplement information — enabling easy and fast location of desired material. Additionally, visitors to the new site can find information relevant to their specific position by choosing from the tabs on the right side of the screen, which include manufacturers, regulators, healthcare professionals, patients/consumers, and members/volunteers. Featuring the latest updates and news on USP's publications, events, and issues, the new homepage now makes the site's most newsworthy content easier to locate. Additionally, the new website has been expanded to offer all of its content in Mandarin Chinese, Portuguese, and Spanish, and also provides more information on USP's international and regional activities, exchange programs, and the USP Medicines Compendium. Available at: www.usp.org.

HerbalThink-TCM is an interactive game and database software designed to help "health professionals and students learn the ancient art of traditional Chinese herbal medicine." Created by scientists and computer engineers at the Rocky Mountain Herbal Institute (RMHI) in Hot Springs, Montana, the program encourages users to use critical thinking and deliberation as opposed to simply repeating memorized facts. RMHI's director, Roger Wicke, PhD, intended for the program to complement the nature of traditional Chinese medicine, which is individualized and personal to each unique patient. By serving as a study guide, quiz, and lecture, the program teaches users how to ask their patients targeted questions in order to identify their true underlying imbalances and create an appropriate herbal formula. It features Chinese herbology references and study guides, clinical "puzzles," video simulations, data on more than 430 herbs, legal information, and more. HerbalThink-TCM is available for purchase by all interested persons, not just students of RMHI, and has received positive reviews from leading herbalists such as Paul Bergner. Available at: www.rmhi-herbal.org/herbalthink/index.html.

NIH Clinical Research Trials and You is a new website from the US National Institutes of Health (NIH). Because clinical trials — which can lead to the approval of life-saving medicines — cannot be done without volunteer participants, NIH created the online resource to give the public a better understanding of this often-unknown community. According to NIH, "research has shown that among the greatest challenges to recruitment of volunteers is the lack of general knowledge about what trials involve, where they are carried out, and who may participate." The new website provides information on clinical trial participation, volunteers' experiences, researcher input and explanations, and links to clinical trial searches. Healthcare professionals also will find guidance on talking to patients about clinical trial participation, as well as promotional and educational materials. Available at: www.nih.gov/health/clinicaltrials/.

Classifieds

Publications

American Herb Association Quarterly Newsletter: $20/yr. AHA, P.O. Box 1673, Nevada City, CA 95959.

Australian Journal of Medical Herbalism: Quarterly publication of the National Herbalists Association of Australia (founded in 1920). Deals with all aspects of Medical Herbalism, including latest medicinal plant research findings. Regular features include Australian medicinal plants, conferences, conference reports, book reviews, rare books, case studies, and medicinal plant reviews. AUD/$95 plus AUD/$15 if required by airmail. National Herbalists Association of Australia, 33 Reserve Street, Annandale, NSW 2038, Australia.

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

Other

American College of Healthcare Sciences, ACHS.edu is the only accredited, fully online college offering degrees, diplomas, and career-training certificates in complementary alternative medicine. ACHS is committed to exceptional online education and is recognized as an industry leader in holistic health education worldwide. Visit www.achs.edu, call (800) 488-8839, or stop by the College campus located at 5940 SW Hood Ave., Portland OR 97239.

Get Certified with ABC's Herbal Information Course. This self-paced online course is designed to help retail employees and multi-level distributors communicate knowledgeably with customers about herbs and dietary supplements. After successfully completing the course, you'll receive an Herbal Information Specialist Certificate and a window decal announcing "Herbal Information Specialist On Staff." Renewable annually. $69.95 Bulk pricing available. www.nutrilearn.com.

Interns, get hands-on experience before you graduate! If you're a future pharmacist or dietitian, you can choose a rotation through ABC's internship program. You'll get a comprehensive introduction to phytomedicines, researching the medicinal, culinary and cosmetic uses of herbs, answering ABC members' questions, working with medicinal plants in ABC's 2.5 acres of herbal gardens, and preparing herbal salves, tinctures or meals. For more information, call 512-926-4900x114 or e-mail education@herbalgram.org.

Stock Photography that doesn't look like Stock: Steven Foster Group, Inc. Photography, Consulting, Publications. Specializing in medicinal and aromatic plants, along with the places they grow, our stock photo files include more than 120,000 images shot around the world for over 30 years. Contact us at our location in the heart of the Ozarks in Eureka Springs, Arkansas. Visit our website: www.Stevenfoster.com or email: sfoster@Stevenfoster.com.

Considering supplying herbal products in Europe? Ann Godsell Regulatory can offer consulting advice on regulatory strategy, and data requirements. Services for dossier preparation & submission also available. For more information email regulatoryinfo@anngregulatory.eu.

North American Institute of Medical Herbalism. Now accepting applications for Introductory, Advanced, Clinical, Nutrition, and Flower Essence programs in the Vitalist Tradition. In-depth training in the theory & practice of Western Herbalism and Nutrition. Fundamentals course begins August 6, 2012. Contact Lisa Ganora 720-722-4372. NAIMH.com

Considering supplying herbal products in Europe? Ann Godsell Regulatory can offer consulting advice on regulatory strategy, and data requirements. Services for dossier preparation & submission also available. For more information email regulatoryinfo@anngregulatory.eu.

Yes, I want to SUPPORT ABC

Join:

Online - **www.herbalgram.org**

Phone - **1-800-373-7105**

Mail – Complete and send this form to: ABC
P.O. Box 144345
Austin, Texas, 78814-4345

AMERICAN BOTANICAL COUNCIL

- ☐ Individual — $50*
- ☐ Academic — $100*
- ☐ Professional — $150*
- ☐ Nonprofit Organization — $250*
- ☐ Corporate — $500*
- ☐ Sponsor
  (Contact Denise Meikel at denise@herbalgram.org or (512) 926-4900 ext. 120)

* (Add $20 postage for international delivery for above levels.)

Payment instructions

Charge credit card (Visa or MC only)

_____

exp. date: _____

(Please include the 3-digit number following the account # on signature line on back of card.)

_____

- ☐ Send invoice to the address below
- ☐ Check enclosed

_____
name

_____
company

_____
profession/title

_____
phone fax

_____
e-mail

_____
address

_____

_____
city state/province

_____
zip country

- ☐ Do not share my contact info
- ☐ Do not send me the e-mail newsletter

Individuals, organizations, and companies support ABC through membership

The AMERICAN BOTANICAL COUNCIL Invites You To *Join Us*

The American Botanical Council is the leading nonprofit education and research organization using science-based and traditional information to promote the responsible use of herbal medicine.

Founded in 1988, the member-supported American Botanical Council:

- SERVES members in more than 81 countries worldwide
- EDUCATES consumers, healthcare professionals, researchers, educators, industry and the media on the safe and effective use of medicinal plants
- ADVOCATES responsible herbal production and use
- ADVISES the media on emerging herbal science
- PROMOTES a healthier world through responsible herbal use.

Join Us!

In return, you'll receive access to a wealth of herbal data via:

- ABC's acclaimed quarterly journal, HerbalGram
- 7 online databases of herbal information (depending on membership level)
- Regular electronic updates on herbal news that matters to you
  - 12 monthly HerbalEGrams and 360 HerbClips per year, plus other Member Advisories
- And much more.

Learn more at
www.herbalgram.org
or contact Denise Meikel at denise@herbalgram.org or (512) 926-4900 ext. 120.

AMERICAN BOTANICAL COUNCIL

How we help your products **grow.**

Good news for health food producers: It doesn't take long to acquire more than 80 years of experience in botanical derivatives, an impressive scientific track record and ingredients of clinically documented activity. All you need to do is prefer Indena brands in your formulations. We now have ten of these, and the presence of one of their logos on your packaging is a guarantee for your customers of the excellence of what's inside. To know more, contact Indena today. And find out how we can make your business grow faster.

indena
science is our nature®

www.indena.com
Headquarters - Indena S.p.A. - Viale Ortles, 12 - 20139 Milan, Italy - tel. +39 02.574961
Indena Biotechnology (Shanghai) Co., Ltd - Unit 03, 16/F, Cross Tower, 318 Fu Zhou Road - Shanghai 200001 - China - tel. +86.21.22815900
Indena France S.A.S. - 23, Rue de Madrid - 75008 Paris - France - tel. +33 1 45229128
Indena Japan Co., Ltd. - KDDI Bdl. 21F. 1- 8-1 Otemachi- Chyoda-Ku Tokyo 100-0004 - Japan - tel. +81.3.3243 9924
Indena USA Inc. - Two Union Square, 601 Union Street, Suite 330, Seattle, WA 98101 - USA - tel. +1.206.340.6140