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In this issue of the *AHPA Report*

Inside AHPA

AHPA Committees Further Association's Mission: Expo West Meetings Update

by Anneli Spielman

Many of the American Herbal Products Association's (AHPA) committees were hard at work at Natural Products Expo West this past March, supporting the organization's work in the regulatory, quality, scientific, and education arenas.

The AHPA committee system provides the structure in which members are able to collaborate on a wide range of projects that are essential to the advancement of the manufacture, distribution, and marketing of herbal products. Many of AHPA's initiatives are derived from ideas born in its committees.

Michael McGuffin, AHPA's president, says the breadth and diversity of AHPA's committees are representative of the membership and industry at large. "Some of our committees, such as the Standards Committee and the Botanical Raw Materials Committee, are almost as old as AHPA itself and although formed many years ago still have relevance for AHPA's members," he says. "At the same time, the AHPA board is always open to new requests and so has chartered two new committees, the Cannabis Committee and the Sports Nutrition Committee, just in the past year. As the interests of our members evolve, so does the organization, as we exist to serve our members' needs," he adds.

Committee members reap the rewards of contributing to positive progress within the herbal products industry as well as contributing to the work of AHPA. Suzanne Shelton, president of Shelton Group Public Relations and chair of the Communications Committee, says that her committee "helps AHPA tell its story and through the annual AHPA Awards, honor those who make significant contributions … but more importantly, the committee helps the association educate its members."

The committees provide valuable information and tools to AHPA members, says Michael Schaeffer, president of Pacific Nutritional Inc. and co-chair of the Standards Committee. He notes that his committee is involved in establishing standards, guidelines, test methods, research data, and other educational resources in understanding government regulations that affect the industry.

In addition, Michael Lelah, PhD, technical director of NOW Foods and chair of the Analytical Labs Committee, says his committee provides members with information on analytical methods critical for suppliers and manufacturers of dietary supplements and other consumer products.

Education Committee Chair Beth Lambert, CEO of Herbalist & Alchemist Inc., voices the sentiments of many when she says, "It is terrific to work with such a talented group of industry and professional members who are so generous with their time."

Committee Updates from Expo West Meetings

Below are highlights and news from AHPA's committee meetings held at Natural Products Expo West in Anaheim, Calif., March 10-13. Also included are highlights from the board meeting of the AHPA-ERB Foundation. Information about all of AHPA's committees is available online. Simply log in as a member to view minutes from past meetings and to access member-only documents.

Analytical Laboratories Committee

The committee discussed modifying existing and adding additional information on known adulterants listed in the AHPA Guidance Policies. It also introduced a beta version of a wiki-type forum for botanical identification beginning with microscopy and provided updates on the shelf-life guidance document and other white papers. In addition, the group discussed identity testing of proprietary flavors that are sometimes single chemical compounds.

Ayurvedic Products Committee

The committee suggested that AHPA provide information through the Ayurvedic Drug Manufacturers Association (ADMA) to make

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sure Indian exporters understand California's Proposition 65. The committee also discussed the possible impact of the European Union's Traditional Herbal Medicinal Products Directive (THMPD) and heard from Alban Maggiar of the French association SYNADIET, who provided his thoughts from the perspective of a European organization that has been intimately involved in this emerging regulation.

Botanical Raw Materials Committee

Updates were provided on the *Organoleptic Analysis of Herbal Ingredients White Paper*, the Tonnage Survey, and the *Botanical Safety Handbook*. The Non-Timber Forest Products Subcommittee reported on interactions with the Indiana ginseng coordinator. Research into sustainable harvest practices for osha in Colorado were discussed as was the need for a microbial reduction white paper.

Cannabis Committee

The committee recognized that it would be useful to compile information about any existing standards for limits on tetrahydrocannabinol (THC) levels in hemp products and evaluate whether the committee can provide guidance in this matter for food-form cannabis products. The committee also formed a working group to address appropriate labeling, including nutrition labeling of medical marijuana in food forms in states where this is allowed.

Chinese Herbal Products Committee

The Chinese Herbal Products Committee discussed topics relevant to the potential impact of the EU's THMPD on continued availability of Traditional Chinese Medicines (TCM), as well as the decision by the International Organization for Standardization (ISO) to create a standard for TCM. The committee recommended that the US delegation attend the next ISO meeting, to be chaired by Michael McGuffin, AHPA president, and support naming the relevant ISO committee as "Traditional Chinese Medicine."

Communications Committee

The committee recommended that AHPA's communications department survey members on their web use and collect and prepare bids for presentation to the board for the July 2011 meeting to revise the AHPA website. Discussion around the need to recuse committee members from the process of voting on award winners and around the formation of a formal nomination process will be considered at a future meeting. Also, a working group was formed to research what deliverables a revised Request for Proposal will include and other aspects of marketing of the upcoming revision to the *Botanical Safety Handbook*, which will likely include a subscription-based e-book and a mobile phone application.

Education Committee and Small Business Committee

The committees discussed the development of seminars and pro-

cesses, including the Microscopy Course, which Rutgers University had agreed to host and which had been scheduled for May 7-8, but which was delayed until the fall of 2011. The combined group then discussed seminar topics that were identified for potential development, including FDA Good Manufacturing Practice (cGMP) Inspections and Emerging Issues, New Food Safety Law and Hazard Analysis Critical Control Point (HACCP) Implementation, New Dietary Ingredients (NDI), cGMP Compliance Series, Organoleptic Analysis, Botanical Garden Tour/Herb Walk at Expo West 2012, Certificate of Analysis (CoA) Development and Working With Suppliers, and "Best Practices" Guide for small businesses.

Government Relations Committee

The committee agreed to form working groups to address numerous emerging regulatory issues that may affect AHPA members' businesses. This committee also discussed the Obama administration's Executive Order 13563 which, among other things, requires all federal departments to identify how their regulations can be "more effective or less burdensome," and FDA's small entity guide for 21 CFR 111 (cGMP).

Sports Nutrition Committee

The Sports Nutrition Committee discussed the 100+ notices brought under California Proposition 65 by a single plaintiff, the Environmental Research Center, that is targeting diet shakes and large-format supplement products, such as protein powders. The committee was also given the opportunity to preview a draft of the website to keep the issue of drug-spiking in front of industry, which had been reviewed and undergone revisions by a working group of the committee. Geranium oil and the possibility of it containing the compound 1,3-dimethylpentylamine (or its related compounds/synonyms) and labeling issues related to these ingredients were also covered by the committee.

Standards Committee

The Standards Committee discussed the current guidance policy on residual solvents as well as appropriate microbial limits for herbal tea. USP nomenclature issues were covered, and the committee was informed that the USP Pharmacopeial Forum is now free online.

AHPA-ERB Foundation

The foundation board welcomed Elan Sudberg as the foundation's newest member and welcomed back Lyle Craker, Jim Fischer, Jim Kinsinger, and Mary Beth Watkins, each appointed for three-year terms. The board adopted a charter for a Research Review Committee, which will identify, develop, review, and recommend botanical research to be supported by the AHPA-ERB Foundation. Any AHPA member may make research suggestions by contacting Steven Dentali at sdentali@ahpa.org. The foundation board discussed amending the foundation's bylaws, primarily to revise the process whereby the board chair is selected, and to make minor administrative revisions. It was reported that a final manuscript for the

second edition of the *Botanical Safety Handbook* is nearing completion and is currently projected to be submitted to the publisher later this year. Finally, the board discussed the significant progress being made on creating a web-based program or wiki that will make out-of-copyright botanical identity text available as an open-source resource.

McGuffin Represents US Botanical Trade at CITES Plants Committee Meeting

The 19th meeting of the Plants Committee of the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES) was convened in Geneva, Switzerland, in mid-April, both to address issues raised at the most recent Conference of the Parties (CoP 15) and to prepare for the next CoP, scheduled for 2013.

CITES is an international agreement that came into force in 1975 and now includes 175 countries, known as Parties to the Convention. CITES functions by maintaining three separate lists, called Appendices, of internationally traded plant and animal species that have been identified as subject to the protection of the Convention, and the Parties voluntarily take on responsibilities for monitoring and controlling such species. These responsibilities include regulatory controls for both importation and exportation of these species.

"The herbal industry shares many goals with the CITES community," says Michael McGuffin, American Herbal Products Association (AHPA) president, who represented the US botanical trade at the committee meeting. "Preservation of plants in trade has relevance not only to governments and environmental groups, but also to herb companies and their customers."

The Plants Committee this week addressed several topics related to species identified as medicinal and aromatic plants. One report provided recent annual trade data for American ginseng (*Panax quinquefolius*), goldenseal (*Hydrastis canadensis*), and pygeum (*Prunus africana*), among others. These and dozens of other plants in the herbal supplement and cosmetics trades are listed on CITES Appendix II, such that international trade is allowed so long as such trade is not detrimental to the survival of the species. Species in the more restrictive Appendix I may only be traded internationally if cultivated.

The Plants Committee also discussed a policy that exempts finished products that contain certain listed species from CITES controls, and reviewed programs used to evaluate how well its regulatory processes are working for a number of species. It focused also on ideas for building the capacity of countries around the world to make good decisions in implementing CITES rules, and for assisting customs agents in their border inspection responsibilities.

"My attendance at CITES meetings always aims to share industry experience so that pragmatic programs are developed," McGuffin says. "At the same time, I am actively involved in the committee's working group to make sure that AHPA and its members stay informed about any and all CITES developments that can impact the herbal trade."

AHP's Microscopy Text Now Available with 10 Percent AHPA Member Discount

The American Herbal Pharmacopoeia's (AHP) *Botanical Pharmacognosy Microscopic Characterization of Botanical Medicines* has just been published by CRC Press. The text, compiled by some of the world's most knowledgeable experts, provides microscopic descriptions of more than 140 medicinal plant species currently in trade, with detailed text and graphic descriptions of each of these and their possible adulterants. Production of the book was funded in part through a grant from the National Institutes of Health Office of Dietary Supplements (ODS).

This seminal work provides information that is essential to any company that uses microscopic analysis to identify its herbal ingredients. The 140+ plants in the text represent 90 percent of the dollar value of botanical sales in the United States. The text covers not only plant anatomy, but it also provides instruction on how to set up a microscopy lab and prepare, view, and archive whole and powdered plant parts for microscopic analysis. Additionally, the text is much more than a microscopy tome, as its introductory chapters provide detailed reviews of botanical nomenclature, adulterations, and diagnostic characters of plant parts. It is an invaluable training tool for quality control personnel that goes far beyond microscopy.

Under federal current good manufacturing

practice (cGMP) regulations, dietary supplement manufacturers are required to conduct at least one test or analysis to verify the identity of each of the herbal ingredients they use.

"This text is an essential reference for herbal manufacturers at this time of increased cGMP scrutiny," says Michael McGuffin, president of the American Herbal Products Association (AHPA). "For companies that purchase herbal ingredients, especially in powdered form, microscopy may be the most affordable tool for meeting their cGMP identity verification requirement." McGuffin has served as a volunteer board member of AHP for many years.

The AHP microscopy text is now available to AHPA members at a 10 percent discount from its retail cost of $169.95. To order, contact AHP.

"The work of AHP is solely based on creating a strong foundation of quality control for the herbal products market and provides direct benefit to all of AHPA's members," notes Roy Upton, executive director of AHP and the lead editor of the new microscopy text. "The genesis of this work arose from discussions in AHPA's Standards Committee meetings and would not have materialized without the efforts of AHPA President Michael McGuffin, who secured partial funding for it through ODS. In this regard, this text is the shared work of AHP and AHPA and is a testimony of what we can accomplish when working collaboratively."

To learn more about the microscopic identification of botanicals, AHPA is offering a 2-day, hands-on, educational training to assist both manufacturers and suppliers in establishing identity. The AHPA seminar, Microscopic Identification of Popular Botanical Materials, to be held in the fall of 2011, provides participants the experience necessary to conduct microscopic analysis on a variety of popular botanical ingredients.

New Members

TCM Product Inc. provides services to companies that have their own formula, want to enhance a current formulation, or would like to create a custom private label. TCM Product advises, develops, and manufactures at a cGMP-compliant facility in partnership with Fair Trade Certified vendors that offer the finest raw materials.

Bent Creek Institute Inc. (BCI) is a 501(c)(3) non-profit business incubator conserving and developing western North Carolina's unique plant biodiversity assets by anchoring our nation's emerging integrative wellness economy through science in botanical quality and safety. BCI is a program of The North Carolina Arboretum, an affiliate of The University of North Carolina.

Apollo Herbs is a business dedicated to the art and science of herbal medicine and offers herbal elixirs, serums, oils, syrups, and aromatherapy roll-ons. By growing, harvesting, and extracting healing plants, we seek to provide the community with the highest-quality herbal products available. All of our products are

made in small batches using the highest-quality organically grown or wild-harvested plants available. Apollo Herbs are skillfully formulated and produced by botanist and natural product chemist Michael Steven Ford.

Golden Biotechnology Corporation is an innovative biotechnology company in Taiwan, specializing in researching and developing innovative health care products, including a novel fungus, *Antrodia camphorara*. Founded by Sheng Yung Liu in 2002, GBC is an innovative drug discovery and herbal supplement company dedicated to enhance lives by developing high-quality products that prevent and treat diseases. GBC aimed to discover new drugs, especially in the anti-cancer and anti-atherosclerosis areas, from screening platforms during 2002-2004. GBC continuously develops its pipeline of new drugs and is currently expanding into new drug development.

Savings Opportunities for AHPA Members

Within the pages of this edition of *AHPA Report*, we are pleased to provide our members with several valuable money-saving opportunities. The following goods and services are offered at a discount for—or are uniquely available to—AHPA members this month:

- American Herbal Pharmacopoeia, *10% off for AHPA members* (page 19)
- AHPA's *Herbs of Commerce, special price for AHPA members* (page 23)
- CPG Jobs, 15% off for employers (page 13)
- First National Merchant Solutions, *members-only offer* (page 6)
- The Tan Sheet, *$360 off of new subscriptions* (page 8)

Legal & Regulatory

What the Warning Letters Teach: A Demand for Compliance

by Anthony L. Young, Esq., Partner, Kleinfeld, Kaplan and Becker LLP, and AHPA General Counsel

The Food and Drug Administration (FDA) Warning Letters are instructive because they disclose those matters that FDA has determined it would follow through on if the company receiving the letter does not come into compliance. A Warning Letter is a demand for compliance.

The American Herbal Products Association (AHPA) notifies its members about Warning Letters for dietary supplements and botanical food products in Legal Alerts because these letters provide key information about the agency's enforcement priorities. Any regulated industry wants to see where enforcement occurs. Why? Because these industries are generally compliant with regulatory mandates, and those companies operating outside the regulatory boundaries are competing unfairly by using unlawful methods to sell their products.

With every large-scale natural disaster, including the recent earthquake and resultant tsunami in Japan, the US marketplace seems to be flooded by quick cures and "complete" protections offered by the dietary supplement and other industries. In this case, FDA quickly alerted consumers—and in so doing, it also alerted the supplement industry—about products fraudulently making claims regarding exposure to radiation-emitting materials from the damaged nuclear reactors. Despite fair warning, two dietary supplement companies made unlawful claims for their potassium iodide products and thus were each the recipient of a Warning Letter: Eidon Inc. and KT Botanicals LLC.

On another note, the April 6 Warning Letter to Omega Nutrition USA teaches the vagaries of FDA inspections. The company received only one warning with respect to good manufacturing practice (cGMP). The letter stated that Omega Nutrition's master manufacturing records were not compliant—the company was using a recipe-calculator sheet in lieu of detailed specifications and controls for each product. Later, FDA identified structural failures in the design of the facility, as well. The Warning Letter also noted that products did not bear the term *dietary supplement* and that the company website made numerous drug claims for products.

Saw Palmetto Harvesting Co. received a Warning Letter after FDA performed a desktop inspection of the company's website. Claims that products will address erectile dysfunction and address benign prostatic hypertrophy resulted in a Warning Letter. Putting those claims on a website makes a company an easy target for a desktop inspection by FDA.

It is unlawful to make unapproved drug or health claims for foods. So, labeling sprouts and mung beans and other foods as potent anti-tumor agents or as reducing the risk of breast cancer resulted in a Warning Letter, as Jonathan's Sprouts Inc. found out. Moreover, unapproved antioxidant and vitamin-nutrient-content claims also deserved a warning in FDA's view. This letter is instructive in that it demonstrates when nutrient content claims may and may not be made.

A similar Warning Letter went to Diaspora Tea & Herb Co. LLC with respect to unlawful drug and nutrient content claims. Dietary supplement companies need to be attentive to nutrient-content-claim regulations and requirements. Such claims are not the highest FDA priority, but when FDA sees that they are being made, the agency will act as it did in these cases.

It is important for even the most experienced companies to assure that relevant personnel are reading and familiar with FDA Warning Letters. Following the AHPA Legal Alerts is one way to do so. AHPA members can sign up their employees for these alerts by providing names and email addresses to Devon Powell via email. In this fashion, both new and old, and experienced and inexperienced employees can keep up to date with FDA enforcement activities.

FDA Holds Meetings on Import Provisions of New Food Safety Law

by Merle Zimmermann, AHPA Information Analyst

The Food and Drug Administration (FDA) held public meetings on March 29 and March 30-31 on how FDA should implement certain sections of the Food Safety Modernization Act (FSMA). The FSMA, enacted in January 2011, is the most significant overhaul of federal food law since the passage of the Federal Food, Drug and Cosmetic Act in 1938.

A primary theme of the new law is to emphasize prevention of food contamination by establishing new practices in food manufacturing. New rules that result from the law will apply to all food sold in the United States, including imported food. Dietary supplement companies are exempt from some parts of the law, and these exemptions also apply to both domestic and foreign firms. (See the *AHPA Update* of Dec. 20, 2010.)

The focus of the meetings was on the pending implementation of some of the elements of FSMA Title III, Improving the Safety of Imported Food. More specifically, the March 29 meeting was titled, FSMA and Imports: A New Paradigm for Importers, while the March 30-31 meeting was called, Ensuring the Safety of Imported Foods and Animal Feed: Comparability of Food Safety Systems and Import Practices.

The meetings provided an opportunity to discuss FSMA Section 301 (Foreign Supplier Verification Program), which, as of January 2013, will require all food importers to verify that the foods they import are manufactured in compliance with US laws and are not adulterated. Sections 302 (Voluntary Qualified Importer Program), 305 (Building Capacity of Foreign Governments), and 307 (Accreditation of 3rd-Party Auditors) were also addressed in some detail. Representatives from FDA explained that the latter section will require accredited auditors to notify FDA of conditions that "could cause or contribute to a serious risk to the public health," during both regulatory and consultative audits, and welcomed further comments and suggestions to clarify the exact scope of this section of the law.

During the meetings, FDA staff stressed the risk-management nature of the new law, which requires FDA to efficiently use its resources and focus testing and regulation efforts on high-risk foods and food ingredients while continuing to monitor low-risk products at a lower rate.

Throughout the meetings, the agency stressed that it would respect all US trade obligations to treat foreign producers and importers on an equitable level with domestic producers. It also communicated its understanding of the potential impact of new costs on small businesses and stated its intention to minimize these while still meeting its goals. FDA also promised that any new importer requirements would be clearly announced well in advance of compliance dates.

"It is reassuring to see FDA's commitment to cooperation and communication with industry," notes AHPA President Michael McGuffin. "This new law is going to meaningfully change the way that food importers operate, and it is essential that we pay attention to the agency's implementation strategies."

An archived webcast of the March 29 meeting has been released by FDA. The agency says it is preparing transcripts of both events.

FDA Convenes Second FSMA Meeting: Preventative Controls of New Food Safety Law; AHPA Plans Comments

by Merle Zimmermann, AHPA Information Analyst

The Food and Drug Administration (FDA) continued its series of educational meetings to discuss components of the Food Safety Modernization Act (FSMA). An April 20, 2011, session focused on Preventative Controls.

A primary theme of the new law is to emphasize prevention of food contamination by establishing new practices in food manufacturing. New rules that result from the law will apply to all food sold in the United States, including imported food. Dietary supplement companies are exempt from some parts of the law, and these exemptions also apply to both domestic and foreign firms. (See *AHPA Updates* of Dec. 20, 2010 and April 15, 2011.)

The focus of this meeting in the ongoing series was Preventative Controls, a topic in FSMA Title I, *Improving Capacity to Prevent*

Food Safety Problems. Preventative Controls are used by facilities to identify and address hazards associated with specific foods and food processes and discussed in FSMA Section 103. Two main themes recurred through the meeting: risk assessment for individual products and how facilities can learn about and apply preventative controls in their own manufacturing business.

At the meeting, FDA representatives inquired what industry in each field considers "high risk" and "low risk" food products and ingredients, noting "We were intentionally vague in what we said ... [to allow industry to] ... categorize foods [itself]." FDA's goal to leverage preexisting organization and knowledge in fulfilling its food safety goals was especially clear in this area, and the agency said it welcomes comments on how best to define high and low risk products.

In answer to inquiries about FDA releasing guidance documents to better explain the terminology in the law and intentions of the regulation, the agency embraced this idea and offered to prepare particular documents immediately after inquiries were received. Also mentioned were possible educational guidance documents showing general examples of how preventative controls and Hazard Analysis Critical Control Point (HACCP) requirements apply in actual situations. FDA also stated that it would consider guidance documents from international bodies such as Codex Alimentarius during development of new regulations.

The agency expressed interest in working with industry in conducting safety training for small businesses to further compliance goals, though it had no clear comments when it was suggested FDA accredit domestic third-party educational and auditing programs for that purpose.

FDA reiterated its desire for information on preventative-control best practices from existing large businesses and trade associations.

"FDA's continued commitment to involving industry in the regulatory process is refreshing," says American Herbal Products Association (AHPA) President Michael McGuffin. "As this new law impacts policy and procedure from seed to shelf, FDA's desire for businesses and trade associations to be integrally responsible for our own regulatory frameworks will allow for minimal disruption to industry while meeting FSMA's new prevention goals.

"AHPA remains committed to ensuring the highest quality and consumer confidence in dietary supplements and manufacturers, and we intend to participate in the FSMA implementation process throughout its development," he adds.

FDA is accepting general written comments on FSMA through June 30, 2011, and AHPA's Government Relations Committee continues to review the process in the interim. Please contact Michael McGuffin if you have any suggestions or would like to participate in AHPA's review.

The FDA website for the April 20 event includes an agenda, and FDA indicates that a copy of the webcast will be made available for viewing there as well.

FDA Recall Identifies Whey Protein Supplier; Peppermint, Soy, Ginger, and Chili Powders Also Recalled

The April 6 FDA Enforcement Report identifies a recall for just under one million pounds of whey protein by Bongard Creameries, in Perham, Minn., because the whey ingredient "may have been contaminated with *Salmonella*." Two associated recalls of products containing Bongard's whey ingredient are also noted.

This action formally identifies Bongard as the previously unidentified whey protein supplier likely involved in three voluntary recalls of supplement products in March by Nutrition Express, VitaLabs, and Universal Nutrition. For more information, see the *AHPA Update*, dated March 30, 2011.

In its weekly report, FDA also announced four recalls of organic peppermint-leaf products. Three of these are clearly identified as consisting of "peppermint tea leaves initially recalled by Aromatics, Inc. [Mesa, Wash.] because it has the potential to be contaminated with *Salmonella*;" the fourth is also being recalled for potential *Salmonella* contamination though the supplier is not named.

Additional recalls are noted for several supplement products distributed by Biosan Laboratories Inc. due to the presence of undeclared soy and bulk lots of tea-bag cut ginger and organic chili powder distributed by High Quality Organics, due to a customer report of a positive test for *Salmonella*.

For more information on these recalls, visit the FDA website.

Industry Hosts First Dietary Supplement Caucus Briefing for the 112th Congress

The Congressional Dietary Supplement Caucus (DSC), in cooperation with the leading trade associations representing the dietary supplement industry—the American Herbal Products Association (AHPA), the Natural Products Association (NPA), the Council for Responsible Nutrition (CRN), and the United Natural Products Alliance (UNPA)—held its first briefing for the 112th Congress on April 6. A capacity crowd of 60 House and Senate staffers attended this event.

"AHPA is pleased to be part of this cooperative process, and to provide information to Congressional offices to keep them well informed on supplement issues," says Michael McGuffin, AHPA president.

The luncheon briefing featured Mark Blumenthal, founder and executive director of the American Botanical Council. "I'm truly grateful and honored for this invitation to talk about how safe and beneficial dietary supplements support the health of our citizens and save our nation billions in health care costs each year," says Blumenthal. "The excellent turnout among Congressional staffers demonstrates the increasing interest in and importance of

dietary supplements on Capitol Hill."

Among the key points of Blumenthal's presentation:

- Half of all Americans use dietary supplements, according to the *Journal of Nutrition.*
- Dietary supplements are regulated as foods under the Dietary Supplement Health and Education Act of 1994 (DSHEA).
- The industry has a strong record of self-regulation, including:
  - AHPA's establishment of standards for nomenclature and guidelines for safety
  - CRN's multi-year grants to the Council of Better Business Bureaus' National Advertising Division to help ensure truthfulness in supplement advertising
  - NPA's good manufacturing practices (GMP) program and training seminars
  - UNPA's GMP training initiative, some initiatives co-led with the University of Mississippi
- Dietary supplements have an outstanding safety record, with government statistics showing they are one of the safest categories of consumer products.

Additional briefings will be scheduled on Capitol Hill. This was the first briefing for the 112th Congress and the ninth in a series of briefings since the DSC launched in 2005.

The DSC was recently re-launched for the 112th Congress. The caucus serves as a bipartisan, bicameral group of members to facilitate discussions among lawmakers about the benefits of dietary supplements, provide tips and insights for better health and wellness, and promote research into the health care savings provided by dietary supplements.

In addition, the caucus brings Congressional attention to the role of supplements in health promotion and disease prevention, and addresses the regulation of the supplement industry. Sens. Orrin Hatch, R-Utah, and Tom Harkin, D-Iowa, and Reps. Dan Burton, R-Ind., Jason Chaffetz, R-Utah, Jared Polis, D-Colo., and Frank Pallone, D-N.J., serve as co-chairs of the caucus.

New Regulatory Challenges the Subject of FDA-Orange County Regulatory Affairs Educational Conference

The Food and Drug Administration (FDA) has announced the 14th Annual Educational Conference co-sponsored with the Orange County Regulatory Affairs Discussion Group (OCRA). The conference, June 8 and 9, 2011, in Irvine, Calif., is intended to provide the drug, device, biologics, and dietary supplement industries with an opportunity to interact with industry experts and FDA reviewers and compliance officers from the centers and District Offices.

This interactive conference will focus on product approval, compliance, and risk management in the three medical product areas. Industry speakers, interactive Q&A, and workshop sessions will also be featured to encourage open dialogue on challenging regulatory issues.

The conference will be held from 7:30 a.m. to 5 p.m. at the Irvine Marriott hotel in Irvine, Calif. Registration will cover refreshments, lunch, materials, and parking. Registration is $725 for members, $775 for non-members, and $475 for FDA/government/students.

See OCRA's website for registration and meeting information, or contact Linda Hartley, Office of Regulatory Affairs, FDA, 949.608.4413, or the Orange County Regulatory Affairs Discussion Group, Attention to Detail, 949.387.9046.

Botanical Science Update

by Steven Dentali, PhD, AHPA Chief Science Officer

Presentations and Meetings

10th Annual Oxford International Conference on the Science of Botanicals

I attended the 10th Annual Oxford International Conference on the Science of Botanicals (ICSB), held in Oxford, Miss., April 11-14, and sponsored by the National Center for Natural Products Research (NCNPR) within the School of Pharmacy at the University of Mississippi. As always, this conference hosts a rich environment as the best annual US conference for industry regarding botanical science opportunities and information. It functions to review, discuss, and explore the confluence of current research topics in natural product chemistry, pharmacognosy, and botanicals by focusing on academic, industrial, and regulatory perspectives.

I chaired the poster session, selected judges, and oversaw the review of and awards for the best student posters. This year's $750 award winners were Meriem Ouchfoun of the Université de Montréal, Yelkaira Vasquez of the University of Mississippi, and Paola Ordóñez from the University of Arkansas for Medical Sciences. I also participated in a panel discussion focusing on current issues surrounding botanicals that fielded questions from the audience.

The ICSB conference is supported by a cooperative agreement between the NCNPR and the Center for Food Safety and Applied Nutrition (CFSAN) at the US Food and Drug Administration. It is co-sponsored by the Shanghai Institute of Materia Medica/CAS, China; the Council of Scientific and Industrial Research (CSIR - India); the Ministry of Indigenous Medicine, Sri Lanka; the American Society of Pharmacognosy; the Society for Medicinal Plant and Natural Product Research; and the Korean Society of Pharmacognosy. Unfortunately, several FDA employees of CFSAN were unable to travel due to funding uncertainty. The conference was well attended nonetheless!

The European Situation

Opening the first session, "Current Status of Science and Regulations of Botanicals in Europe," Gerhard Franz, PhD, from the Universität Regensburg in Regensburg, Germany, gave a talk titled "Up-to-Date Development of Herbal Drugs and Herbal Drug Preparations in the European Pharmacopoeia." He discussed terminology differences, pointing out that the terms *herbal drug* and *herbal drug preparations* are in the 2010 *European Pharmacopoeia 7.0* (EP), while the term *botanical* is not officially used. He also mentioned that the EP standards apply to all medicines regardless of origin and that the 2010 two-volume EP that was implemented last year contains 2,300 monographs and now has a separate "Herbal Drugs and Herbal Drug Preparations" section. These monographs total 178 and 80 examples, respectively, in the seventh edition, which is up from 123 and 61 monographs in the sixth edition. The increase is partly due to the addition of 15 monographs on Traditional Chinese Medicines (TCM).

Dr. Franz pointed out that the United States doesn't yet have observer status at the European Pharmacopoeia Commission, and he discussed the situation for herbal drugs in Europe by reviewing the regulatory categories of Traditional Herbal Drugs and New, or Well Established, Herbal Medicinal Products. He clarified that *herbal drug* is synonymous with the term *herbal substance* as used by the European Community legislation on Herbal Medicinal Products.

He also explained that herbal preparations can be obtained by subjecting herbal drugs to processes such as extractions and include extracts, essential oils, and expressed juices. He noted that powdered herbs are much less used now than herbal extracts, and he defined Standardized, Quantified and Other extracts, and native vs. not-native extracts, being those that also contain technical excipients.

Dr. Franz defined Standardized extracts as extracts that have constituents with known therapeutic activity, such as a belladonna leaf dry extract, while Quantified extracts have a defined range of active markers, such as St. John's wort extracts. A third category, Other extracts, were defined as essentially process defined but which may have a defined minimum of analytical markers as with some valerian extracts. Regarding the 75 TCM-candidate monographs for the EP, it was conceded that not all of the analytical requirements, such as having defined marker compounds for Other Extracts, may be appropriate.

The identity tests in the new EP include macroscopic, thin-layer chromatography (TLC), and microscopic, alongside new tests for aflatoxins, ochratoxin, residual solvents, heavy metals, and aristolochic acid. Colormetric assays have been changed to liquid chromatographic (LC) methods.

In considering the future of TCM herbal drugs in the EP, Dr. Franz categorized them as single chemicals, complex mixtures, and Traditional Herbal Medicine as clinically used. He closed by noting that global collaboration is needed between the European Union (EU) and interested countries in order to make continued progress on harmonized monograph development.

Wolfgang Blaschek, PhD, from the Institute of Pharmacy in the Department of Pharmaceutical Biology at the University of Kiel in Kiel, Germany, followed with a talk titled "Herbal Medicinal Products: Regulatory guidelines for Efficacy and Safety in Europe."

He discussed the European situation regarding all medicinal products, including Herbal Medicinal Products and the criteria for their marketing authorization of quality, safety, and efficacy in order to assess their risk-benefit analysis.

Dr. Blaschek explained that the European Medicines Agency (EMA) is a decentralized agency of the EU responsible for the scientific evaluation of medicines. Its management consists of a member and an alternate from 27 member states, making up six committees, including one for Herbal Medicinal Products. He discussed marketing access and the requirements for applications that include full applications, bibliographic applications, and mixed applications. He also covered Traditional Herbal Medicinal Product (THMP) applications and simplified registrations for which plausible efficacy can be shown on the basis of bibliographic data.

He also discussed the present situation where THMPs legally on the market have had a 7-year grace period prior to their required registration at the end of April 2011. A mutual recognition procedure was discussed whereby applicants receiving marketing authorization in one member state could market that product in all member states. The aims and responsibilities of the Committee for Herbal Medicinal Products (HMPC) were introduced as was the Community List of herbal substances, preparations, and combinations for use in THMPs.

Dr. Blaschek stated that the HMPC monographs are comprised of harmonized scientific opinion and also explained the different requirements between Well Established Use applications and THMP ones. He said that the European Scientific Cooperative on Phytotherapy's *ESCOP Monographs*, created by an umbrella organization of national scientific phytotherapy associations, and the 116 WHO medicinal plant monographs may also be helpful to industry. He closed by reminding the audience that the risk from most herbal medicine products is relatively low compared to other drugs but that pharmacovigilance regarding their use is still important.

Rudolph Bauer, PhD, from the Karl-Franzens-University Graz in Graz, Austria, speaking on "Chinese Herbal Medicine in Europe: Regulatory Situation and Scientific Evaluation," discussed the determinations of these products as medicinal products or dietary supplements regarding applications using the EU regulatory framework. In the EU, food supplements are intended for health purposes providing a nutritional or physiological effect. Claims must be substantiated by studies and, like in the US, only health claims, and not disease claims, are allowed. With regard to novel foods and novel food ingredients, Dr. Bauer used the example of *Gynostemma pentaphyllum* (jiaogulan) in Germany, where it is considered as a novel food and sold as a type of tea.

Dr. Bauer also defined herbal medicine products as used for treating or preventing disease and THMPs as having limited applications, along the lines of those for over-the-counter drugs, and requiring a minimum of 30 years of use, of which 15 years must be in the EU. He also discussed challenges in the quality control of Chinese herbal preparations that include substitutions and adulterations, mixtures containing a high number of different herbs, the difficulty of obtaining authentic samples, and the fact that therapeutically relevant compounds in the herbs are often unknown. On top of that, the

influence of different processing methods is not well known, and reference compounds are often lacking, all of which indicate the need for more research!

Dr. Bauer discussed the European prohibition of aristolochic acid-containing herbs and that the EP has TLC and high performance-liquid chromatography (HPLC) tests for aristolochic acid in herbal drugs. He mentioned the limit for external exposure of pyrrolizidine alkaloids of 100 mcg/day and the internal one at not more than 1 mcg/day. With regard to commonly used angelica species, he mentioned that TLC can differentiate them and that the spread of Chinese traditional herb use and herb preparation is now global. In a response to a question about Indian herbs, Dr. Bauer mentioned that there is a strong focus on herbal quality, safety, and efficacy in India but, unlike China, India does not have observer status at the European Pharmacopoeia Commission. He stated that in Europe overall herbal medicine is being discussed much more and that there is a higher acceptance of herbal medicines now than in recent years.

Chinese Input

On Tuesday morning, De-An Guo, PhD, of the Shanghai Institute of Materia Medica in Shanghai, China, spoke generally about Chinese herbal medicine, describing how formulation strategy begins with yin and yang considerations and employs herbs in combination by their assignment to different roles represented by emperor, minister, assistant, and servant positions. He stated that this approach began empirically from examining a patient's face, taking their pulse, making a diagnosis, and then providing a formula. The medical theory now underpinning it was developed later to include about 12,000 herbs, of which 500-600 are commonly used.

In quantifying the commitment to Chinese medicine by the Chinese government, Dr. Guo said that about $333 million has been committed and that this number will soon practically double. The Chinese Ministry of Scientific Technology and its National Science Foundation are involved in this effort. He reported that a delegation of 15 Chinese were in attendance at the conference. Dr. Guo discussed the Chinese Pharmacopoeia (CP), reporting that of the three volumes published every five years, the first volume is devoted to TCM. The 2010 CP edition provides multiple means to control quality, as assessing single marker compounds cannot do it.

Dr. Guo explained that Chinese regulations are very difficult to comply with and separate products into pure compounds, herbal fractions, and herbal mixtures. He added that the Chinese herbal products industry is making great strides with more than 1,000 TCM manufacturers, the biggest of which may have sales up to $1 billion a year. Most are small manufacturers that may disappear or merge with other companies in order to survive in the face of new regulations that focus on quality standards and new drug approvals. He closed by announcing the 2011 International Conference on TCM Pharmaceutical Analysis, to be held July 1-3, 2011, in Chengdu, China. The theme of the event is "Standardization and Globalization of TCM."

Ling-Yi Kong, PhD, of the China Pharmaceutical University in Nanjing, China, presented a talk titled "Cytotoxic Triterpenoid Constituents from Two Plants of Family Meliaceae" that focused on the application of LC and mass spectrometry (MS) methods in the isolation and structure identification of plant secondary metabolites. He was followed by Dao-Feng Chen, PhD, of the Fudan University in Shanghai, China, who spoke on "Isolation and Characterization of Anti-complementary Agents from Medicinal Plants." During questioning, it was pointed out that there are significant amounts of money spent in China on botanical research, but so far the work of the different research institutes isn't coordinated.

Improved Curcumin Absorption

Stefano Togni, PhD, from Indena S.p.A. in Milano, Italy, presented a talk titled "Development and Clinical Validation of Meriva®, a Lecithin-Based Formulation of Curcumin" that is also the subject of a literature citation in this *AHPA Report*. On average, the phospholipid combination provided a 30-times increase in curcuminoid-plasma concentrations but a 60-fold increase in demethoxycurcumin, which may be a more potent anti-inflammatory compound than pure curcumin. Dr. Togni also discussed two osteoarthritis studies using this material, one of which involved 100 patients over 8 months taking a gram per day dosage.

US Concerns

The later morning session saw Mark Blumenthal of the American Botanical Council speaking on "Quality Control and Economically Motivated Adulteration of Botanical Raw Materials, Herbal Extracts, and Essential Oils in the Global Marketplace," in which he discussed the issue of purposeful adulteration. He credited the American Herbal Products Association's (AHPA) work in this area. He mentioned issues with solvent residues, and adulteration concerns with grapefruit seed extract, goldenseal, bilberry, black cohosh, ginkgo, pomegranate, and saw palmetto oil.

Loren Israelsen, executive director of the United Natural Products Alliance, provided a talk titled "A 20-Year Retrospective on the Progress of Botanical Supplement Regulation in the United States." In this talk, Israelsen supplied a brief history of supplement regulations, the rise in negative media, the appearance of cheap products, Chinese products, doping, social media, online healthcare communities, such as www.patientslikeme.com and www.dailystrength.org, the *New England Journal of Medicine* article titled "American Roulette – Contaminated Dietary Supplements," quality logo mania, new or old dietary ingredients, little botanical drug progress, limited healthcare and professional acceptance, botanical identity confirmation, and FDA funding and enforcement capability. It was, of course, both cogent and entertaining.

California District Attorney

In the Tuesday afternoon session on "Regulatory Aspects of Botanicals," Daryl Roberts, JD, of the Napa County District

Attorney's Office in California, gave a talk titled "Regulation of Dietary Supplements: A Local Law Enforcement Perspective." He spoke about the review for claims substantiation, stating that the Dietary Supplement Health and Education Act (DSHEA) did not define the level of evidence required in making claims. He also pointed out the difference between the Sherman Antitrust Act and California Proposition 65 by explaining the latter as a right-to-know statute that doesn't protect customers from acute risks to health and safety, which is the job of the former. Rick Kingston, PharmD, of SafetyCall International PLLC in Bloomington, Minn., then presented "Are Botanicals Safer after Passage of Regulations for Mandatory Adverse Event Reporting in the US?" He raised the question of safety as being relative and provided a review of the calls received by his organization.

Indian Medicinal Plant Use

Ranjit Puranik from Shree Dhootapapeshwar Ltd. of Mumbai, India, gave a talk titled "Medicinal Plant Consumption in India: Reading the Data," covering the developments of the last 10 years with a focus on the growth of the scope of the National Medicinal Plants Board (NMPB). He stated that there are 500,000 acres under conservation and an equal amount for contract cultivation under NMPB projects with mass scale "Mission Mode" programs for endangered medicinal plants. He presented the NMPB vision statement of herbs as sustainably sourced from organically certified forests and farms, with documentation supporting traceability and legal procurement, in full compliance with fair trade guidelines.

Puranik discussed a survey of 600 manufacturers regarding herbal use. He reported that a total of 752 species were considered, resulting in a total herbal consumption of 80,000 tons, from which 397 species account for less than 10 tons. Only 10 species were reported as listed under the *Convention on International Trade in Endangered Species* (CITES). He provided two examples of reported harvests, namely 19 kgs of *Euphorbia neriifolia* (milk spurge or snuhi) and 71 tons of *Nardostachys jatamansi* (jatamansi) under cultivation. He also reported that the biggest users of these plants are not traditional medicinal plants manufacturers, but rather, large-scale exporters of raw materials, extracts, and phytochemical molecules. There is no tracking of this tonnage that involves 9,000 manufacturers, he said.

Puranik discussed that the average manufacturer may use over 100 species, and he spoke of the need to employ good agricultural and field collections practices. He also spoke about states' organizations and joint forest-management committees that are trusts and societies of all forest tribal communities, whereby trade of what he called "forest produce" would be only through community trusts. He emphasized the need to attend to the use of certified species, and the importance of quality medicinal plant resources, chain of custody, and proper labeling practices. In closing, he mentioned the need to

develop input-output ratios for wild collections that take into account the plant's natural regeneration cycle.

US: Expert Panel, NCCAM, Research, Whole Herbs, and Analysis

Following a break, a panel discussion chaired by John Cardellina II, PhD, from the Office of Dietary Supplements at the National Institutes of Health, with Blumenthal; Israelsen; Duffy MacKay, ND, VP, Scientific & Regulatory Affairs for the Council of Responsible Nutrition; and me as panelists, fielded a wide range of questions from the audience.

Josephine Briggs, MD, director of the National Center for Complementary and Alternative Medicine (NCCAM), kicked off Wednesday's program with a talk titled "Natural Product Research at NCCAM: Current Priorities." She referenced NCCAM's legislative mandate to support basic and applied research and the integration of alternative treatment, and noted that about half of NCCAM's $128 million annual budget funds such research. She discussed the lessons learned from previous trials, including where doubts have persisted regarding the efficacy of St. John's wort, echinacea, and ginkgo, and covered the promise of turmeric as an anti-inflammatory agent in light of a recent article published in the *British Medical Journal* that showed an increased cardiovascular risk from the use of nonsteroidal anti-inflammatory drugs. Briggs emphasized that definitive testing of the efficacy of natural products and finding answers on their safety requires expertise in pharmacology and pharmacognosy.

Birgit M. Dietz, PhD, from the University of Illinois-Chicago in Chicago, next spoke on "Cancer Preventive Properties of Botanical Dietary Supplements used in Women's Health with an Example of Hops and Black Cohosh," followed by Dennis B. Lubahn, PhD, of the University of Missouri-Columbia in Columbia, Mo., who discussed "What's New from the 'Elderberry Center,' also Called the Missouri University Center for Botanical Interaction Studies." Dr. Lubahn's botanical research center has again received 5-year funding after a 5-year hiatus. He spoke on a range of topics, including investigations regarding picrorhiza (*Picrorhiza kurroa*) for potential use for strokes as well as studies on soy, garlic, and elderberry with regard to prostate cancer, strokes, and immune system effects while attending to sourcing, identification, chemical analysis, transgenic animal models, and signaling systems studies.

Floyd "Ski" Chilton, PhD, of the Wake Forest Center in Winston-Salem, N.C., presented an interesting talk titled "Impact of Common Variants in Genes that Synthesize/Metabolize Fatty Acids on Levels of Inflammatory Fatty Acids in Subjects of African and European Ancestry," where he showed clear significant genetic variations of polyunsaturated fatty acid metabolism in human populations. Bill Helferich, PhD, from the University of Illinois at Urbana-Champaign, followed with a talk titled "Botanical Estrogens: Mechanism, Dose, and Target Tissues," where he suggested that isoflavones and equol may increase breast cancer metastasis from bone to lung.

Wendy Applequist, PhD, of the Missouri Botanical Garden in St. Louis, spoke Thursday morning on "Morphological Assessment of the Identity of Selected Unprocessed Botanicals in Commerce." She began by emphasizing that the potential for adulteration or confusion between plants is plant (taxon) specific and related finding a recent lot of skullcap (*Scutellaria lateriflora*) herb that contained germander (*Teucrium chamaedrys*) herb. Applequist explained the material chain of custody and said that, generally speaking, wildcrafters and farmers see the whole material and pass it on to wholesalers and processors, who provide ingredients to manufacturers.

Dr. Applequist explained that herbs sold in the whole form that end up in herb shops are a minority of botanical materials sold. Whole herbs purchased this way are inexpensive and allow users to make their own custom formulas. Additionally, some herbs are not available as finished supplements and buying them whole may help avoid some types of adulteration. She asked the question, "Is the substitution of botanicals by incorrect species a problem for unprocessed herbs on the retail market?" and then presented the results of a project where herbs sold in whole or broken forms were intentionally selected to maximize observed adulteration. Herbs were ordered from retailers selected across the US by focusing on those subject to adulteration either by substitution of the wrong species or ones where unofficial related species were also used, namely skullcap, star anise, chamomile (sometimes adulterated with related genera with higher allergenic potential), St. John's wort, schisandra, juniper, linden (sometimes adulterated with unofficial species), arnica, hawthorn (species are used interchangeably), and chaste tree (can include related species).

Applequist found that some herbs were never adulterated while others almost always were, though toxic adulterants were not found. Juniper berry material was found to often contain fruit of other species in small amounts. Three schisandra samples had fruits of another species that may be used interchangeably in Chinese herbal medicine. Most samples of linden flower had other species mixed in and most of the arnica flower samples were not flowers of *Arnica montana* but instead most likely false arnica (*Heterotheca inuloides*) used in traditional Mexican herbal medicine. Applequist ended her talk by stating that most unprocessed herbs are properly identified, though some species are suspect. She suggested that it would be interesting to see a chemical survey of commercial arnica products to determine what species were used as ingredients in the processed finished products.

Michael L. Eason, PhD, of the University of Texas at Austin in Austin, Texas, provided an interesting talk titled "Ex situ Plant Conservation in Texas and the Ethical and Sustainable Harvesting of Plant Material in the Southwest," about his work with the Lady Bird Johnson Wildflower Center focusing on the access to and difficulties of plant collection. His talk was followed by one from Alain Touwaide, PhD, and Dssa Emanuela Appetiti, PhD., from the Institute for the Preservation of Medical Traditions in Washington, D.C., titled "Old Herbs New Remedies; Toward a New Paradigm," discussing the challenges of gleaning herbal information from 800 BC – 1650 AD by reading ancient books. In order to be useful, texts

must be available electronically, and the information contained within meaningfully organized. The linguistic problems with this work were discussed as well as the importance for the organized information to be standardized and verifiable.

Amy Eichner, PhD, from the US Anti-Doping Agency in Colorado Springs, Colo., gave a talk titled "The Athlete's Dilemma - Discerning Risk in Dietary Supplements," during which she discussed the agency's proposed launching of the Support of Online Resources and Tools (SORT) as a way to inform athletes about product quality and third-party testing. One suggestion she had for industry was for companies to consider sharing their FDA facility-audit results in a way that would be accessible to end-user customers.

John Travis, PhD, of NSF International, discussed the safety of products from the standpoint of the potential presence of illegal products in a presentation titled "Contaminants and Adulterants: Techniques to Unmask the Culprits." Within the realm of anabolic steroids, diuretics, drugs of abuse, and stimulants, he gave specific analytical examples of analyzing for each of these drug categories. He stated that so far, in the phosphodiesterase type 5 (PDE5) inhibitor class of drugs, 20 analogues of sildenafil have been reported and five each of vardenafil and tadalafil. Travis said he will be looking next to broad, non-targeted screening while facing the problem of hard-to-find reference compounds. He pointed out the analytical difficulty of finding what is not supposed to be in a product when you don't know what it is and the general problem of working with complex matrices.

Melissa Phillips, PhD, from the National Institute of Standards and Technology (NIST) in Gaithersburg, Md., spoke on "NIST Tools for Quality Assurance in Botanical Dietary Supplement Measurements" and explained the differences between standard or certified reference materials, which can be used for their certified value, reference value, and information value, and standard reference materials (SRMs) that can be used for equipment calibrations. The institute's matrix-based SRMs made from crops are processed and should not be used as calibrants. She also discussed NIST's Dietary Supplement Laboratory Quality Assurance Program that now has 60 participants that participated in its last exercise. The breakdown of participating labs is approximately one-third 3rd-party testing laboratories, one-third industry labs, and one-third government and other interests.

Once again the ICSB demonstrated great value for the range of content and quality of the talks, the networking opportunities, and overall significance for botanical science issues of interest to industry. The dates for next year's meeting are April 16-19, 2012. I suggest you mark your calendars now!

Literature Citations

Individual TCM Herbal Treatments Rigorously Tested

Flower A, Lewith G, Little P. Combining rigour with relevance: A novel methodology for testing Chinese herbal medicine. *J Ethnopharmacol*. 2011 Mar 24;134(2):373-378.

The clinical practice of herbal medicine often involves the administration of individualized preparations. This is a drawback for conducting randomized, double-blind, placebo-controlled clinical trials that are relevant to actual practice. This feasibility study provided either a placebo or an individualized Chinese herbal preparation to participants, thereby combining the practice of TCM with a rigorous clinical trial design.

Treating Chronic Disease with TCM

Jiang M, Zhang C, Cao H, Chan K, Lu A. The role of Chinese medicine in the treatment of chronic diseases in China. *Planta Med*. 2011 Apr 6. doi:10.1055/s-0030-1270983 [Epub ahead of print]

Traditional Chinese medicine, which accounts for about 20 percent of Chinese health care, is seeing increasing use in treating chronic disease in China. This review examines its importance relative to the Western medical approach, evidence of its safety and efficacy, and approaches to patient classification and determining mechanisms of action of complex herbal mixtures with a view toward the integration of traditional Chinese medicine in health care worldwide.

Galactagogue Herbal Tea Effects

Turkyılmaz C, Onal E, Hirfanoglu IM, Turan O, Koç E, Ergenekon E, Atalay Y. The effect of galactagogue herbal tea on breast milk production and short-term catch-up of birth weight in the first week of life. *J Altern Complement Med*. 2011 Feb;17(2):139-142.

This clinical trial studied whether drinking a traditional German galactagogue instant tea would have any effects on breast-milk production and infants' weight-gain pattern in the early postnatal period. It provides some positive, useful human-safety and efficacy data for a typical, traditional, German herbal-tea formulation in a sub-population of nursing mothers. The herbal tea is actually a dried extract in the form of water-soluble instant granules that are stirred into hot water. The list of ingredients from the manufacturer's website in order of predominance are as follows: sugar, maltodextrin, extracts of hibiscus flower, fennel fruit, rooibos herb, lemon verbena leaf, raspberry leaf, fenugreek seed, and goat's rue herb, vitamin C, and fennel fruit essential oil.

Beneficial Effects Seen with Long-Term Guaraná Use

Krewer C, Ribeiro EE, Ribeiro EA, Moresco RN, Ugalde Marques da Rocha MI, Santos Montagner GF, Machado MM, Viegas K, Brito E, Cruz IB. Habitual intake of guaraná and metabolic morbidities: An epidemiological study of an elderly Amazonian population. *Phytother Res*. 2011 Feb 22. doi: 10.1002/ptr.3437. [Epub ahead of print]

The results described in this study suggest that habitual guaraná ingestion contributes positively to the prevention of various metabolic disorders in the elderly.

Artichoke and Bean Extracts for Satiety

Rondanelli M, Giacosa A, Orsini F, Opizzi A, Villani S. Appetite control and glycaemia reduction in overweight subjects treated with a combination of two highly standardized extracts from Phaseolus vulgaris and Cynara scolymus. *Phytother Res*. 2011 Feb 10. doi: 10.1002/ptr.3425. [Epub ahead of print]

This study reported the results of a randomized, double-blind, placebo-controlled clinical trial performed in 39 overweight subjects for changes in satiety with the administration of extracts from artichoke and common bean. The results were significant, suggesting that this treatment may be potentially useful in the management of overweight.

Green Tea Reduces Fat and Protein Digestion in Rats

Bajerska J, Wozniewicz M, Jeszka J, Drzymala-Czyz S, Walkowiak J. Green tea aqueous extract reduces visceral fat and decreases protein availability in rats fed with a high-fat diet. *Nutr Res*. 2011 Feb;31(2):157-164. (article requested)

This rodent study sought to determine if green tea cardiovascular benefits could be conferred at a dosage that did not impair protein digestion. Cardiovascular risk factors were improved for rats that consumed 1.1 percent and 2 percent green-tea water extract in a high-fat diet, and a significant decrease in body fat and weight gain were seen at the higher exposure, though impaired protein digestion was found at both dosages.

These researchers demonstrated a dose-dependent reduction of body-weight gain and fat accumulation in rats fed a high-fat diet that were also ingesting the human equivalent of 5 or 8 cups of green tea per day compared to control animals. However, this beneficial effect, as well as improvements in blood lipid profiles, was accompanied by some inhibition of protein digestion.

The researchers did not find a mechanism of action for these beneficial effects, and it is not known how significant the apparent reduction in protein digestion was. It is not yet known if this happens in people, but that possibility may help guide the design of future human clinical trials that study green tea for its health benefits.

Curcumin Better Absorbed as Phospholipid Complex

Cuomo J, Appendino G, Dern AS, Schneider E, McKinnon TP, Brown MJ, Togni S, Dixon BM. Comparative absorption of a standardized curcuminoid mixture and its lecithin formulation. *J Nat Prod*. 2011 Mar 17. doi:10.1021/np1007262 [Epub ahead of print]

This study compared the plasma concentrations of curcuminoids from a standard curcumin mixture and from a commercial phospholipid formulation (Meriva from AHPA member company Indena) in nine volunteers using a randomized, double-blind, crossover study design. The average absorption of curcumin from Meriva was increased about 18-fold over the non-phospholipid formulation while the demethoxylated curcumin levels were found to be 50 to 60-fold higher, resulting in a higher concentration of demethoxycurcumin (shown to be more potent than curcumin in anti-inflammatory assays) in plasma than curcumin.

Coumarin Absorption from Cinnamon: Clinical Trial

- Abraham K, Pfister M, Wöhrlin F, Lampen A. Relative bioavailability of coumarin from cinnamon and cinnamon-containing foods compared to isolated coumarin: A four-way crossover study in human volunteers. *Mol Nutr Food Res.* 2011 Apr;55(4):644-53.

The German Federal Institute for Risk Assessment has confirmed a tolerable daily intake of 0.1 mg/kg body weight for the substance coumarin, and the European Flavourings Directive stipulated a limit of 2 mg/kg in food for this naturally occurring substance. Concerns have been raised about the consumption of coumarin by type II diabetics from cassia cinnamon (*Cinnamomum aromaticum*), which contains high levels of coumarin relative to that of Ceylon cinnamon (*Cinnamomum verum*). This study examined the human metabolism of 12 mg of coumarin from 1) coumarin in a capsule, 2) cinnamon capsules, 3) cinnamon tea, and 4) cinnamon rice pudding, finding more rapid absorption and higher peak exposure to coumarin from cinnamon tea than the other samples. A statistically significant finding, but not important from a risk-assessment perspective, was the slower absorption of coumarin from ingestion of the cinnamon capsules.

Plant Aphrodisiacs Reviewed

- Melnyk JP, Marcone MF. Aphrodisiacs from plant and animal sources—A review of current scientific literature. *Food Res Int.* 2011 Mar 5. doi:10.1016/j.foodres.2011.02.043. [Epub ahead of print]

This review assessed the current scientific literature for evidence of the sexual-enhancing properties for several botanicals including Asian ginseng (*Panax ginseng*), "horny goat weed" (*Epimedium* spp.), maca (*Lepidium meyenii*), muira puama (*Ptychopetalum olacoides*), tribulus (*Tribulus terrestris*), yohimbine (an alkaloid from yohimbe, aka *Pausinystalia yohimbe*), and others including nutmeg, saffron, and chocolate (cacao). The authors conclude that the potential exists for many of these to be used as aphrodisiacs but that more research is needed to establish their function in humans, including clinical trials, before definitive conclusions about their effectiveness can be drawn.

Review of Phytochemical Databases

- Scalbert A, Andres-Lacueva C, Arita M, Kroon P, Manach C, Urpi-Sarda M, Wishart D. Databases on food phytochemicals and their health promoting effects. *J Agric Food Chem*. 2011 Mar 28. [Epub ahead of print]

The content and limits of over 50 phytochemical databases are reviewed in this article that discusses their utility and directions for future improvements.

Green Tea Leaves and Supplements: Differences Revealed

- Sun J, Chen P, Lin L-Z, Harnly JM. A non-targeted approach to chemical discrimination between green tea dietary supplements and green tea leaves by HPLC/MS. *J AOAC Int*. 2011 Mar;94(2):487-497.

Sophisticated chemical analysis employing HPLC/MS and chemometric software determined that significant differences exist between green tea supplements, particularly liquids, and green tea samples. Additionally, unlabeled additives were found in some samples. The Office of Dietary Supplements and the Agricultural Research Service of the USDA supported this work.

Yerba Mate Spray Dried: Chemical and Antioxidant Evaluation

- Berté K, Beux M, Spada PKWDS, Salvador M, Ribani RH. Chemical composition and antioxidant activity of yerba-mate (Ilex paraguariensis A.St. Hill., Aquifoliaceae) extract as obtained by spray drying. *J Agric Food Chem*. 2011 Apr 21. doi:10.1021/jf2008343

Spray-dried water extracts of herbs normally brewed as tea may provide a tea alternative for herb use as a food or supplement ingredient. This study found higher levels of polyphenols and caffeine, and a lack of fiber, in the water extract of yerba mate compared to yerba mate leaves. Antioxidant activity consistent with high polyphenol content was also measured.

Cranberry Product Analytical Method Single Lab Validated

- Brown PN, Shipley PR. Determination of anthocyanins in cranberry fruit and cranberry fruit products by high-performance liquid chromatography with ultraviolet detection: single-laboratory validation. *J AOAC Int*. 2011 Mar;94(2):459-466.

A single laboratory validation for the HPLC-UV analysis of the five major cranberry anthocyanins in raw cranberry, cranberry juice, cranberry juice cocktail, and cranberry extract powder is described in this report. Validated according to AOAC International guidelines, the method was also subjected to a stability study and ruggedness trial. The Office of Dietary Supplements and the National Institute of Standards and Technology supported this work.

New Philosophical Approach to Rationalizing Phytotherapy

- Gertsch J. Botanical drugs, synergy, and network pharmacology: Forth and back to intelligent mixtures. *Planta Med*. 2011 Mar 16. [Epub ahead of print]

This thought-provoking mini-review starts off by reminding us that traditional pharmacognosy was reverse engineered to discover pharmacologically active molecules and leads for new drugs. It then asks if botanicals also provide effective mixtures, pointing out that sound experimental data are widely lacking to prove that whole herbs are better than purified chemicals extracted from them. The author suggests that the emerging concept of network pharmacology may be fundamental to understanding and rationalizing botanical use. His review is replete with discussions on mixtures, synergies, the dangers of drug interactions, and polypharmacy. He insists that the study of the pharmacodynamics of botanical drugs is necessary to rationalize phytomedicine use.

Calendar of Botanical Events

- Introduction to Food Science & Technology Course
  Starting May 21 • Los Angeles, Calif. For information, contact Frances J Richmond, PhD.
- NHP Research Society of Canada
  May 24 - 27 • Montreal, Canada
- Institute of Food Technology Food Expo
  June 11 - 14 • New Orleans, La.
- Natural MarketPlace 2011
  June 23 - 25 • Las Vegas, Nev.
- International Conference on TCM Pharmaceutical Analysis
  July 1-3 • Chengdu, China
- International Symposium for High-Performance Thin-Layer Chromatography
  July 6 - 8 • Basel, Switzerland
- 27th International Symposium on the Chemistry of Natural Products
  July 10 - 15 • Brisbane, Australia
- American Society of Pharmacognosy
  July 30 - August 3 • San Diego, Calif.
- International Symposium on Medicinal and Aromatic Plants; History of Mayan Ethnopharmacology
  August 17 - 19 • Flores Petén, Guatemala
- American Association of Naturopathic Physicians Convention
  August 17 - 20 • Phoenix, Ariz.
- Society for Medicinal Plant and Natural Product Research
  September 4 - 9 • Antalya, Turkey
- International Symposium of Essential Oils
  September 11 - 14 • Antalya, Turkey
- Natural Products Expo East
  September 21 - 24 • Baltimore, Md.
- Phytochemicals in Nutrition and Health
  September 27-30 • Bari, Italy
- 3rd International Conference of Bioinformatics, Natural Products and Traditional Medicine
  October 14 - 16 • Xi'an, China
- 5th International Conference on Polyphenols and Health
  October 17 - 20 • Barcelona, Spain
- The Royal Flora Ratchaphruek 2011
  November 14 - 18 • Chiang Mai, Thailand. Program flyer here.
- International Symposium on Medicinal and Aromatic Plants
  November 15 - 18 • Chiang Mai, Thailand
- Phytochemical Society of North America, 50th Anniversary Meeting
  December 10 - 15 • The Island of Hawai`i, Hawaii