

Scientific Approaches to Quality Assessment of Botanical Products

National Center for Natural Products Research (NCNPR), School of Pharmacy, The University of Mississippi, September 7-9, 2004

by Sidney Sudberg, DC, RH (AHG)

Co-organizers Ikhlas A. Khan, PhD, Director of FDA Program and Larry A. Walker, PhD Director for National Center for Natural Products Research (NCNPR) of the School of Pharmacy at the University of Mississippi were hosts to a workshop: *Scientific Approaches to Quality Assessment of Botanical Products*. This workshop was supported through a cooperative agreement between NCNPR and the Center for Food Safety and Applied Nutrition (CFSAN) of the Food and Drug Administration, and co-sponsored by the Office of Dietary Supplements (ODS) of the National Institutes of Health (NIH).

The purpose of the workshop was to review and discuss methods used in determining the identity, purity, quality, and strength of botanicals. Numerous national and international speakers, representing different cultures and disciplines of the science of herbal medicine, addressed issues related to authenticating and assessing the quality of the botanicals and methods involved in their characterization. Speakers were leading researchers from industry, academia, non-profit institutions and government.

This is the third in the series of conferences dealing with various aspects of the safety and efficacy of botanicals. The event brought together an unprecedented array of experts and scientists from many disciplines: taxonomy, chemistry, pharmacognosy, molecular biology, and traditional herbal medicine, which made this truly a learning experience. The unique

blend of speakers and topics addressed the needs of the FDA which is on a 'fact-finding' mission of its own, providing an opportunity for FDA officials to interact with experts on both sides of the herbal fence. Among the 100 attendees were researchers, manufacturers, herbalists, scientists, product developers, conservationists, and botanists. They were able to discuss issues that could only help enlighten all and bring everyone closer to the reality of what Herbal Medicine is to the people who are taking these medicines.

Being in the lush green environment of Oxford, Mississippi with only mild humidity, added to the quality of the four days spent there. The conference opened on Tuesday evening with Robert Brackett, PhD, Director of CFSAN/FDA who spoke about the general issue of quality control and its effect on public safety. As part of the Dietary Supplement Health and Education Act of 1994 (DSHEA), Congress gave the FDA authority to develop and implement mandatory standards or labeling for dietary supplements. The FDA has issued a proposed rule that would require the use of industry-wide standards in the manufacturing, packaging, and holding of dietary supplements, thus reducing the risks associated with contamination from harmful or undesirable substances such as pesticides, heavy metals, or other impurities, or improper labeling which fails to accurately describe what supplements contain.

This raises the issue of testing a starting material or



Sidney began his career in chemistry in 1969 at the City University of NY where he was involved in drug discovery for cancer research, followed by graduate studies at SUNY-Stonybrook and NYU. In 1987 he studied acupuncture and western herbal medicine in the UK. He received his doctorate of chiropractic in 1988 from the Los Angeles College of Chiropractic. In 1997 Sidney created Alkemists Pharmaceuticals, Inc., an independent contract & research laboratory dedicated to dietary supplement analysis.



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a final product that you receive as a manufacturer, whether herbalist or large commercial manufacturer. The question of whether laboratory testing of a product is mandatory was addressed. If you are certain of a product's identity, and you have or can produce documentation that is valid data or information, then no further testing is required. If you are able to rely on your supplier and they can produce documentation that is valid and sufficient to satisfy FDA requirements, be it a paper trail or organoleptic, macroscopic, microscopic, TLC, FTIR, HPLC, MS, NMR, etc., then no further testing is required. On the other hand, if something should go wrong with this product, you would be ultimately responsible for the damages. It is imperative to have all the proper documentation in order and to be confident in your 'data' or at least have an audit/paper trail so that FDA can trace any product clearly to its source as well as the path it took to get there, if it should ever become necessary.

The following morning we began with discussions concerning "Approaches to Establishing Identity," starting with cutting-edge material from Paul But, PhD of the University of Hong Kong (Shatin). Dr. But spoke about 'Approaches to Establishing Identity by Molecular Means.' This well-prepared presentation recognized the validity of the traditional identification of botanicals with organoleptic markers such as size, shape color, taste, and smell. As science progressed, more 'reliable' systematic matching based on external morphological and internal anatomical features evolved and became the standard. The advance of chromatographic technology further allowed comparison of the chemical profiles of botanical materials with those of authentic samples. These approaches, however, focus only on the phenotypic expressions and secondary metabolites, which are very sensitive to environmental influences and thus more variable.

With the advent of molecular biology and more specifically, the introduction of the polymerase chain reaction (PCR) technology, it became possible to zoom directly into the genetic constituents of botanical markers so as to generate markers for identifying them to the source species. The advantage is obvious, as genetic markers are often species specific and not affected by season, age or most environmental conditions. The disadvantages are that this method works best with live

plant material and it won't help identify extracts as well as being susceptible to fungal contamination.

One of the next speakers was Ikhlas Khan, PhD from the National Center for Natural Products Research and Department of Pharmacognosy, School of Pharmacy, University of Mississippi. Dr. Khan spoke on the 'Role of Fingerprinting in Quality Assessment of Botanicals,' offering the possibility that validated methods can insure quality control in manufacturing and storage, and that these should be required tools for optimal efficacy and safety of finished products. His opinion, shared by many of the participants at this conference, was that herbal products cannot be considered scientifically valid if the product tested was not authenticated and characterized in order to ensure reproducibility in the manufacturing of the product in question. Many studies refer to the use of standardized material, but in reality they are referring to chemical standardization. While chemical standardization may be important, its utility is limited when the starting material has not been well characterized botanically. This could be as straightforward as botanical/morphological identification or as elaborate as genetic or chemical profiling.

The fact remains that quality is in the mind and hands of the formulator/manufacturer and the fact is that inconsistencies exist in nature and there is no way of changing that. Therefore, standardization of botanicals as a concept, as it is frequently described by scientists and used by many manufacturers of many of the commercial products, is inconsistent with nature.

Up next on the program was Dean Gray, PhD of the Midwest Research Institute (formerly of Herb Pharm), who spoke on the 'Development of Analytical Methods for Analysis of Complex Crude Materials and Finished Products.' Dr. Gray, recognizing the diversity of dietary supplements and specifically botanicals, acknowledged the limitations of the current state of science when applied to commercially popular botanicals. His presentation provided an overview of the selection, development, and use of appropriate analytical methods for crude materials and finished products to help determine identity and phytochemical quality.

Session Two, "International Approaches to Establishing Quality of Botanical Products," brought together representatives from the United States,

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Germany, India, Canada and Japan. Much of the discussion focused on establishing quality control of these biologically complex materials with a slightly different approach in each case. Some speakers used highly sophisticated instrumentation in their attempt at insuring product safety and efficacy, and some even tried to predict product quality with the more advanced technology. Whatever the focus of any of the speakers, in all cases they seemed genuinely interested in the plants themselves and showed a deep respect for herbs as medicine. It was rarely necessary to remind the speakers and the audience of the reason for being there: the tradition of herbal medicine.

The final session, titled "Approaches to Verifying Purity and Assessing Strength," brought a unique blend of speakers with varied backgrounds. Some of the speakers represented the herbal tradition as we know it. Trish Flaster of Botanical Liaisons spoke on 'Botanicals...They Can't Tell Us Their Name,' an elegant talk that brought us closer to the earth and its relationship with the plants. We were exposed to the world of the voucher specimen which is the ultimate tool to guarantee the identity, purity, quality, and strength of botanicals. It all starts with the voucher specimen, a pressed specimen of the flowering plant. No scientific method can surpass this as the gold standard, at least so far. Genetic species identification even depends upon a voucher specimen to create the unique sequence that is used to identify any future samples. Trish made it abundantly clear that the level of sophistication achieved with the voucher specimen is of paramount importance in this industry and there are no substitutes.

Of the remaining speakers in the program, those who chose a traditional perspective in taking on the difficult question of herb strength were of novel interest to this scientifically oriented crowd. David Bunting of Herb Pharm gave an excellent presentation on 'Strength of Liquid and Solid Botanical Extracts: The Herb to Extract Ratio.' David spoke on the significance of strength ratios and the fact that traditional safety data is based on consistent strength ratios. Herb to extract ratios of the fluid extract vs. tincture were used as examples of the traditional 'standardized' extracts which are the basis of traditional herbal use and the historic safety record of botanicals, enabling subsequent herbalists and other practitioners to prescribe medicine for their

clients/patients with absolute confidence.

Of the remaining speakers, one stands out for her eclectic approach to herbal medicine and the noble task of the assessment of quality. Aviva Romm of the American Herbalists Guild spoke on 'Determination of Botanical Medicine Quality by Herbal Practitioners and Small Manufacturers.' Aviva gave us a synthesis of how quality, therapeutic efficacy, and safety are assessed in the complex blend of traditional practice, observation of therapeutic response, unique experiential knowledge of the plants, and contemporary scientific studies. According to Aviva, unique knowledge of individual plants, organoleptic testing, and therapeutic experience provide an important basis upon which to review the definition of 'standardization.' Her goal is to see cooperation between scientific researchers and botanical practitioners/small manufacturers to present novel approaches to understanding the optimal conditions for growing, harvesting, preparing, storing, and delivering medicinal plant products.

This workshop was a very good start to a potentially bright future for herbal medicine. To have this many researchers, scientists, regulators, and herbal practitioners in one room for two full days is a major accomplishment for one of the speakers and organizers, Joe Betz, PhD from the office of NIH/ODS. Dr. Betz, a pharmacognosist formerly with the FDA, also served as the Vice-President of the American Herbal Products Association. He should be commended for his capacity to bring such a group together on this important topic at this pivotal time. Conventional allopathic medicine is being questioned and challenged more and more. This workshop brought to the forefront of mainstream science the fact that herbal medicine is a fact of life, and will prevail if we stay the course and join forces with science and industry to give them the life that is intrinsic to this nature-based and life-perpetuating discipline.