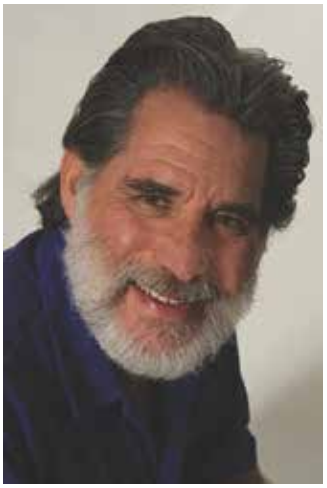
Mark Blumenthal: Quality and Efficacy of Herbal Medicines

Interview by Craig Gustafson



***Mark Blumenthal** is the founder and executive director of the American Botanical Council (ABC), the leading independent, nonprofit organization dedicated to disseminating accurate, reliable, and responsible information on herbs and medicinal plants.*

He is the editor/publisher of HerbalGram, an international, peer-reviewed quarterly journal. For 6 years he was an adjunct associate professor of medicinal chemistry at the University of Texas at Austin, College of Pharmacy, teaching the course "Herbs and Phytomedicines in Today's Pharmacy." Blumenthal is the senior editor of the English translation of The Complete German Commission E Monographs–Therapeutic Guide to Herbal Medicines *(1998),*[1] Herbal Medicine: Expanded Commission E Monographs *(2000),*[2] The ABC Clinical Guide to Herbs *(2003),*[3] *and coauthor of* Rational Phytotherapy *(2004).*[4] *He has appeared on more than 400 radio and television shows and has written more than 500 articles, reviews, and book chapters for many major publications. In 2010 he was awarded the prestigious Tyler Prize in honor of the late Purdue Professor Varro E. Tyler from the American Society of Pharmacognosy.*

Integrative Medicine: A Clinician's Journal (IMCJ): Could you begin by informally describing the mission of the American Botanical Council, or ABC?

Mr Blumenthal: ABC is a science-based nonprofit research and education organization. We are also considered an advocacy organization in the sense that we advocate for a scientific basis for the application of herbs, medicinal plant products, phytomedicines, and related plant-based and fungal-based products in both self-care and in health care. We are particularly interested in those plants and phytomedicinal products that have a clinical research basis to support their rational and responsible use.

At the same time, we are not so scientific that we ignore the historical record, the information that's come down to us through centuries and millennia of empirical use. For example, we respect the traditional medicines of India and China and other traditional societies where there are systematic uses for the various botanical materials. These herbs are usually used in combinations—often based on their perceived energies, as opposed to chemical constituents, which is a more modern way of seeing how plants work and why they have certain activity. What we do is report the emerging science—and, I should say, not just the emerging science, but the exploding amount of scientific and clinical research on medicinal plants and phytotherapeutic agents that have been coming from research centers all over the world in the last 2 or 3 decades.

***IMCJ*:** What objections have been used against published research of herbal medicines?

Mr Blumenthal: People have often said, "There is no research, there is no science on this." That is based on ignorance. Other people have said, "There may be science on this, but the scientific studies are too small, or they are poorly designed." That is true of some of the studies, but a growing body of studies are increasingly well designed and meet the gold standard that people in evidence-based medicine like to apply based on the randomized, controlled clinical trials. There is even a growing body of systematic reviews and meta-analyses of those randomized, controlled trials—a vast body of published reviews, in many cases supporting the safety and the appropriate use of various phytomedicinal products in self-care and in clinical medicine.

This fact gets routinely ignored in the mainstream medical journals and in the mainstream media, not only in this country but in other countries as well. As you and I both know, science and medicine, and science reporting, are becoming increasingly international and global, particularly with the advent of the Internet and Web-based publications. The national borders are less and less important and the domain of various national medical and scientific societies

becomes less important in the sense that people are reading materials that are published in other parts of the world. That is because research—usually in English, the international language of science—is an international phenomenon, as is the global supply chain for many of the botanical ingredients used in these herbal products.

The bottom line for us at ABC is that there is a body of scientific data—clinical research material—that supports the judicious, responsible use of herbal supplements, phytomedicinal products, et cetera, in self-care and clinical medicine. Part of our job has been to report this. If you want to look at the history of it all, ABC helped to pioneer awareness of this research; through our peer-reviewed journal *HerbalGram*, ABC was one of the very first organizations and *HerbalGram* one of the first publications to routinely report on the emerging science—especially the clinical studies on many of what are now some of the most popular herbs in the marketplace: echinacea, ginkgo, milk thistle, saw palmetto, and black cohosh, just to name a few of the more well-studied phytomedicinal products that have enjoyed some significant degree of popularity.

***IMCJ*:** Is there any one particular location that has taken a leading position on recognition and systemizing herbal medicines?

Mr Blumenthal: European phytomedicine is based on a different regulatory structure and the different cultural attitude that exists in Europe, particularly Germany. Back in the 1998, we published the *The Complete German Commission E Monographs: Therapeutic Guide to Herbal Medicines*,[1] a 715-page book of translations of some 385 monographs that were produced by an expert committee of scientists and health professionals who were knowledgeable about herbs and phytomedicines, under the auspices of the German government's counterpart to our Food and Drug Administration. It is known as the BfArM, the acronym for *Bundesinstitut für Arzneimittel und Medizinprodukte,* which translates as the German Federal Institute for Drugs and Medical Devices. It is like the United States' FDA.

At any rate, over a period of years from the late 1970s to the middle 1990s, the German government empaneled this special commission, known as the Commission E, and many people are aware of this because it is a matter of historical record. Many older people in the integrative medicine community will remember the Commission E Monographs. The German government was the leading developed nation with a scientific background in the area of herbs and their medicinal uses. Many people knew back then that German science and medicine and pharmacology was cutting edge. When I was young, in the 1950s and 1960s, if you wanted to study medicine, you frequently had to study *both* Latin and German because so much of the medical and pharmacological literature was in German. That has changed, of course.

The point is that the German government's Commission E evaluated all the available published and unpublished data—some of it submitted by various companies—on close to 400 herbs to determine their safety, efficacy, and suitability to be sold as nonprescription medicines in German pharmacies.

These monographs were basically written as package inserts to help guide patients and health professionals to determine the government-accepted, approved use or uses of this herb were. For example, the definition of the herbal drug, the approved use or uses, recommended dosage, adverse effects, and any known contraindications or drug interactions, et cetera. These were part of the German Federal Register and, until ABC published our book, nobody had ever systematically made them available in English and accessible in a database format.

***IMCJ*:** What was the significance of ABC's efforts to publish these monographs?

Mr Blumenthal: The Commission E Monographs were our contribution to the public's awareness of the benefits of herbs at a very critical time in the 1990s. We started translating and editing in the middle 1990s and it was finally published in a book in 1998. The message was—especially right after the Dietary Supplement Health and Education Act, or DSHEA, was passed—to help professionals, consumers, industry, congress, and regulators realize that we do not necessarily have to reinvent the wheel with respect to determining the relative safety and potential benefits of some of these herbs.

Many of the herbs have been approved as medicines—not as dietary supplements—because their safety is established as well as their suitability or efficacy in clinical practice or in self-medication. It was not just the ABC saying this; it was the German government saying it. This was basically considered the most rational system in the world for evaluating herbs for their safety and efficacy for nonprescription medications. We sold over 20 000 copies of the book and the entire Commission E Monograph is available on the ABC Web site, http://www.herbalgram.org. It is now a benefit of membership in ABC at all levels, whether it is on the consumer individual level, academic level, professional level. or for libraries, industry, et cetera.

The German Commission E Monographs are now being replaced in the European Union by EMA Community Monographs that are produced by experts at the European Medicines Agency on a pan-European basis, with experts from all over the European Union. So, the Commission E Monographs should be seen primarily in an historical context, even though today they are still considered an authoritative reference on the safety and efficacy of herbal drugs at the time in which they were compiled.

Many of these herbs were basically unknown to the average person in this country. Echinacea became popular in the early to middle 1980s in this country. Ginkgo and

milk thistle and some of these herbs—black cohosh, St John's wort—were unheard of until the late 1980s or early 1990s. Then they started getting advertised and promoted in the media. This herbal revolution that we have seen, this herbal interest, is very much consumer led. They are the ones pulling the train in many cases. They are now aided by many health professionals—the naturopathic community being one sector of them and also innovative practitioners who have studied in conventional medical schools but have open enough minds to realize that there are other safe, effective, and appropriate remedies that people can use, whether nutritional, herbal, or otherwise. They are the ones that have been pushing for a more widespread social acceptance and pushing the agenda forward. It has not come from the medical establishment. It has not come from the government taking leadership on this. It has come from the people who are using these relatively safe natural products and who are benefiting from them.

***IMCJ*:** Does ABC publish any other resources on herbal medicines?

Mr Blumenthal: For over 30 years we have been reporting in *HerbalGram* about this growing body of research that in the past was hardly available anywhere else. People just did not know what was going on research-wise. *HerbalGram* was one of the first places people were able to find this information. Nowadays, with the advent of many publications that cover integrative medicine topics, like *IMCJ*, the Internet, e-mail, and all of that, access to such research has become very decentralized. The accessibility of herbal research is a positive development—that is, assuming that people are getting quality, reliable, and responsible information.

Part of the problem is that it is sometimes difficult to differentiate the wheat from the chaff in some of these Internet-based forums. People often put out information that is very supportive of their financial and commercial agenda. Sometimes they try to dress it up or try to legitimize it as if it were some type of scientific or third-party type of Web site, when in fact it is really just a front or an alias for a company and the information may or may not be as accurate or responsible as the viewer believes it to be.

***IMCJ*:** Where might communication regarding herbal medicines still be weak?

Mr Blumenthal: There is so much ignorance about so many of these randomized, controlled trials that have been systematically reviewed and/or meta-analyzed. As most *IMCJ* readers are probably aware, a meta-analysis is basically a systematic review in which there is more homogeneity in one or more of the variables than exist in a systematic review—for example, homogeneity in the actual herbal material being tested, or in the clinical endpoints, or other factors in the trial design. There is an increase in the publication of these reviews with positive results, supporting the herbal product or material that was tested in the clinical trials, and yet this information is not adequately getting communicated to help professionals who would be well advised to know about this.

Knowing more about these positive systematic reviews and meta-analyses might help reinforce their already-existing clinical practice using the reviewed botanical or, if they are on the fence about it, it might help move them toward being more willing to consider at least the clinically-tested botanical preparations in their clinical practice. There seems to be an inadequacy in communicating that kind of information. We try to promote it whenever we can in the ABC HerbClip database and in *HerbalGram* and in many of my presentations to health care professionals. A lot of this information gets lost in the background noise with so much information, misinformation, and over-communication.

***IMCJ*:** Could you discuss what the HerbClip database is?

Mr Blumenthal: HerbClip is our database of over 6000 2- to 3-page summaries—or sometimes, critical reviews—of clinical trials on herbs and phytomedicines as well as systematic reviews and meta-analyses of these trials. We publish 15 HerbClips every 2 weeks, 30 a month. Sometimes HerbClips summarize articles dealing with topics like ethnobotany, regulation, or a laboratory analytical method to detect if adulteration of the botanical material has occurred. We tend to focus on clinical trials, probably 95% of the time, and most HerbClips are peer reviewed.

HerbClips are not just a summary; sometimes they include a comment from a reviewer or correction to an error in the reviewed study. The HerbClip summaries contain much more information than the official study abstract. Such information includes, but is not limited to, a definition that describes the herbal product, such as "a 6:1 extract of the root of the plant," or "containing 45% of these compounds," or whatever it is; the market name of the product; and the name of the company that makes the product. That is an important part of what we strive to clarify in the growing body of herbal scientific information. Conventional pharmaceutical drugs, for example, are usually almost always one single chemical entity—a defined chemical that is specific to one manufacturer because they have a patent on it before it goes generic.

Aspirin is aspirin is aspirin. Ibuprofen is ibuprofen. These are common nonprescription analgesics. Botanicals are chemically complex mixtures of naturally occurring constituents. With extracts these chemicals can be adjusted or normalized to produce what is most commonly referred to as a standardized extract. The standardization process is often conducted to chemically adjust or modify the extract to increase certain actives or decrease—or remove altogether—certain substances that might be considered

potentially toxic or undesirable. Some more simple extracts—for example tinctures or fluidextracts—seldom have any chemical adjustments or standardization.

The point here is that in an ABC HerbClip we provide much more detailed information on the chemical definition of a specific herbal product used in a particular clinical trial being summarized—much more information than is provided in an abstract.

And, by the way, as an aside, it is astonishing to me that some journals still publish clinical trials on herbs and phytomedicines in which virtually no descriptive details are included to give the reader an idea as to what is really being tested in the clinical trial. Without these details, one can consider the trial results next-to-meaningless, and, at the very most, very difficult to compare with other trials on different formulations of the same herb.

***IMCJ*:** Beyond *HerbalGram* and ABC's other publications, do you have any other formal programs that are specifically geared toward educating or informing the clinical practitioner about the efficacy of herbal medicines?

Mr Blumenthal: We did have at one time an Herbal Information Course that was available, based on our third book, *The ABC Clinical Guide to Herbs*,[3] published in 2003. The second book was an expansion of the Commission E Monographs; it was called *Herbal Medicine Expanded Commission E Monographs*.[2] In the clinical guide, we reviewed all the available clinical literature on the top 30 herbs in the market at that time in the United States. To be best of our knowledge ABC was the first party to link the clinical trials on certain herbs and the actual brand name of the product that was used in each of the clinical trials, as well as to define the extract or the product so that people knew what the product actually was.

When discussing these herbs it is important to consider that they are not always generic—they are not necessarily commodities per se. Many clinical research studies are conducted on proprietary, sometimes patented, frequently chemically defined botanical extracts that go by a certain name in Germany or Switzerland and maybe a different name here in the United States or wherever they are being marketed. ABC was possibly the first organization to start banging the drum and letting clinicians, consumers, and others in industry realize that if you are going to say, "I think it might be useful to use ginkgo extract for this condition, or milk thistle extract for that condition," then it is important to ask, "Which ginkgo, which milk thistle, or which other commercial herbal products are we talking about?"

The clinical studies almost always, with some exceptions, tend to be focused on 1, 2, or 3 leading clinically tested phytomedicinal products, often from Europe, although, depending on the herb, they can be from other places as well. As I've already noted, because botanicals are so chemically complex, it is important to make sure people know what kind of material—particularly if it is a commercial brand—was used in this clinical trial.

I am not suggesting that the advent of the clinical trial in the last 50 or 60 years was necessary as a precondition for herbal medicines to have any efficacy. That would be an absurd statement to make because people have been using herbs and medicinal plants for thousands of years before the advent of clinical research. I am saying that reporting on these modern clinical trials is necessary to define the botanical material in the therapeutic setting because botanical A used in trial X could be very different but of the same common and scientific names as company B's product in trial Y. Clinicians need to know what was being used and what this material is. The two herbal products may or may not act the same although they're made from the same herb.

ABC also has a very robust research database called HerbMedPro. HerbMedPro is based on 250 of the top herbs in the marketplace; it is searchable by Latin name or common name. We have compiled all of the PubMed abstracts, abstracts from Cochrane, and any other free-access databases, and each abstract is condensed into a 1-sentence summary and organized into categories based on the type of research—for example, botany, chemistry, pharmacodynamics studies, clinical trials, toxicology, et cetera. If one wanted to look at just drug interactions for a particular botanical, there might be 16 papers published on drug interactions. You click on that and it takes you to a page where we have summarized every one of those 16 drug-interaction papers in 1 sentence with a link to the abstract on PubMed.

If you want to look at clinical trials involving ginkgo, for example, we currently have an astonishing 341 clinical papers on ginkgo and 319 clinical papers on tea—including green tea. Again, these are 1-sentence summaries that make it really easy to understand what that trial is about. Then you go to the abstract, that is, if you want to see the abstract.

***IMCJ*:** The ABC has launched an initiative focusing on adulteration. Can you discuss this program?

Mr Blumenthal: The ABC-AHP-NCNPR Botanical Adulterants Program was started by ABC. We are the founding organization and the managing partner of this. We also work with our partners, the American Herbal Pharmacopoeia, or AHP, which is another nonprofit organization that works on herbal standards and herbal quality, and the University of Mississippi at their National Center for Natural Products Research, or NCNPR. That is an FDA-funded center of excellence where scientists at "Ole Miss" have developed a massive, world-class facility for analysis of medicinal plant products, dietary supplements, et cetera, and development of analytical methods for such analysis. It is internationally recognized as one of the world's leading centers. We started the program in 2010 to educate the industry, primarily, but secondarily to educate health professionals, researchers, and others about this growing

problem called adulteration. It is one of the main messages that we are trying to get to people right now.

The program includes numerous types of publications: (1) adulteration reports in *HerbalGram*; (2) "Botanical Adulterants Monitor" quarterly newsletters, of which we now have published 4; and (3) laboratory guidance documents, or LSDs, which are technical reports for quality control and analytical lab personnel, people in regulatory functions of companies, labs and government agencies, and others. The LGDs help identify which analytical methods are actually suitable for determining the authenticity of various botanical materials and detecting possible adulteration. And (4), very soon—the fall of 2015—we will introduce the "Botanical Adulterants Bulletins," short—approximately 3 pages—documents confirming the adulteration of specific herbs.

A company selling a certain herb in one of their products is required by law to do the required GMP, or good manufacturing practices, testing for identity. If they use a method that is older—or maybe even some of the newer methods—guess what? In some cases, the methods may not be adequately robust or refined enough to be able to detect certain types of adulteration going on in the marketplace today—a type of adulteration that may not have been occurring 5, 10, or 20 years ago when that method was published.

Sometimes they are even pharmacopeial methods—methods that are officially recognized in some countries' pharmacopeias—yet they are still possibly inadequate, depending on when they were developed and published. If a company relies on a possibly outdated methods, it could pass a botanical material or extract and end up buying a ton of it and making hundreds of thousands of capsules of an adulterated product—even though the lab, using the inadequate method, had OK'd it.

These LGDs that we are producing are being seen by people in the herb industry as major contributions to the marketplace. They help companies and their in-house or outside contract laboratories save a lot of time and money.

What does this have to do with health care practitioners? Plenty. We are giving practitioners more information on what is being adulterated so that they can talk to representatives of the companies that produce professional herbal dietary supplement product lines. Many of the people who read *IMCJ* are stocking dietary supplements in their clinical practice and selling or dispensing them. I am not saying that any of the professional brands of herbal supplements are adulterated. What I am saying is there is adulteration going on in the industry and this is a global problem. Health practitioners, from an ethical perspective and on a professional level, need to know what is going on so they can at least check on their supplement suppliers to the professionals' satisfaction.

Just because a line of products is sold in the professional channel does not mean, ipso facto, that it is necessarily any better quality or using any better quality ingredients than some of the similar lines that may be sold in the mass market, or in a health food store, or via mail order or the Internet, or via multilevel marketing channels. As a matter of fact, some companies produce products for multiple channels of the market and some of those products are made in the same manufacturing facilities and use some of the same ingredients.

I am not suggesting that there is a problem in the practitioner channel with adulterated material, but I am saying that not all products sold through practitioners are necessarily better than or going through more quality-control procedures than some of the products sold in other channels—even though some of the vendors would like people to think so.

***IMCJ*:** Is it more of a labeling and distribution-channel differential than an actual product differential?

Mr Blumenthal: In some cases, yes. This has to be considered on a case-by-case basis, but having a professional-looking label on the product does not necessarily mean that the ingredients in that product are any better than some of the products that might be found in the market elsewhere.

For example, some of that so-called bilberry extract in the marketplace is not really bilberry. There is a relatively significant amount of adulteration in the bilberry market, but without a wide-scale testing program of most or all of the bilberry products, it's difficult to assess the degree of adulteration. A practitioner might want to talk to the company from which he or she is buying bilberry extract and ask, "How do I know that you are really selling true bilberry as opposed to other blue-purple pigmented fruit extracts, or even red dye No. 2 and charcoal?" These have been documented as one of the adulterant methods for bilberry extract. The issue with some of these ways of adulterating—in this case, bilberry extract—is based on the premise that some methods can fool some of the older, simpler analytical methods into confirming that it is bilberry as opposed to the more robust methods that are, in this case, made official in some of the national pharmacopeias—for example, the United States Pharmacopeia and the European Pharmacopoeia.

Also, we're publishing soon an extensive 20 000-word primer on understanding analytical methods used for botanicals and other dietary supplements for the nonchemist. In other words, if you are a naturopath, if you are a chiropractor, if you are a medical doctor, if you are a quality-control person at a company, a regulatory person at a company, the president or owner of a company—everybody except for guys in the lab—this will be for you. You see all these acronyms used on labels, Web sites, product brochures, and articles and you do not really know what distinguishes this analytical method from that or why this method is supposed to be better for this particular herb as opposed to that method.

Then there is the highly confusing and unfortunate issue with the New York attorney general going after herbal dietary supplements. The New York attorney general relied solely on DNA barcoding as the only analytical method to support his case. His office sent letters to GNC, Target, Walgreens, and Walmart saying that 80% of their house brand herbal dietary supplement products that the attorney general tested were mislabeled and fraudulent, and, later, in public statements, the attorney general's office also added the possibility that the products may present a public health problem due to what the attorney general's inadequate testing suggested was the presence of contaminants.

These public allegations did not accurately reflect what the true situation was. The claims by the New York attorney general relied solely on DNA bar coding. That test was inadequate and inappropriate to test many of these products that were herbal extracts, not just powdered herbs. Most herbal extracts do not contain the plant's DNA! For dried herbal powders the DNA barcoding test method would have been appropriate, but, even then, DNA barcoding is not the only method that should be used for testing dry herbal powders—not dried extracts—because DNA testing cannot differentiate among different plant parts, as required by the manufacturer to differentiate on product labels—that is, the root or leaf or flower of a plant all have the same DNA!

Because of this, the conversation about herbal adulteration and which analytical method to use became front-page news. There has been lots of discussion on blogs, in newsletters, and at conferences about what is the right method to test these herbs. Some of it came from ABC, as we were one of the first parties with a press release saying, "Hey, problem here. They misused the analytical method."

However, in the main, the New York attorney general's message was generally communicated in the media without very much examination of the issue of his office's misuse of the DNA technology, and great damage was done to what many of us consider is already-waning consumer confidence in this category of products. The bottom-line media message that "herbal supplements cannot be trusted" carried the day, despite our efforts to try to clarify the distinctions here.

Yes, there *are* problems with some herbal dietary supplements. Yes, there *is* adulteration of herbal materials going on—both accidental and intentional. But, the New York attorney general's irresponsible actions did nothing to really clarify issues; to the contrary, it muddled public perceptions and the public debate, although it did have possibly one positive impact: It got the herbal adulteration issue onto the front burner.

There is nothing wrong with DNA bar coding if it is employed properly and also if the test results are checked and confirmed with other appropriate chemical or microscopic testing methods. What must be done in ingredient and product testing is to use a robust range of different types of appropriate analytical methods—multiple tools in the toolbox—rather than relying on just one, like the New York attorney general did with DNA. Because this whole product quality issue has now become front-page news, Rick Liva's series of articles on dietary supplement quality control issues in *IMCJ* has increased in relevance and timeliness, as has the work of ABC, the AHP, and other nonprofits in educating the herb industry and related stakeholders—for example, integrative health professionals, natural product researchers, and others—about the need to question and qualify companies selling herbal supplements.

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