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BOTANICAL QUALITY FEATURE**

# The Complexities of Botanical Quality

by Steve Myers

*“The avaricious man is like the barren sandy ground of the desert which sucks in all the rain and dew with greediness, but yields no fruitful herbs or plants for the benefit of others.”*

– Ancient Greek philosopher Zeno of Elea.

**A**varice, or greed, is one of the main contributors to quality control problems in the botanical industry. Whether saving money by skipping necessary components of quality assurance programs or adulterating materials to either earn more or spend less, cheaters and poorly managed companies are motivated by the financial bottom line.

Given the hundreds of phytochemicals in every herb or plant, as well as the expanded number of uses for botanicals, quality control could seem confusing and overwhelmingly elusive to even the most well-intended companies. However, the tools to maintain the highest quality control of botanical products, as well as to quell most cheats, are readily available. “There are quality control standards/monographs for most of the important botanicals in commerce and their extracted forms,” said Josef Brinckmann, vice president of R&D at Traditional Medicinals. “You may have to go outside the United States to get the information.” He noted in addition to the U.S. Pharmacopeia (USP), his company, which works with 120-plus different botanical ingredients, uses a combination of standards from the European Pharmacopeia (EP), the American Herbal Pharmacopeia (AHP), the Indian Herbal Pharmacopeia, the Pharmacopeia of the People’s Republic of China and the Japanese Pharmacopeia. “All of these sources have hundreds of botanical monographs that provide specific tests for identity—usually at least three tests per botanical: macroscopic identity, microscopic identity and chromatography. Plus, they have all of the purity tests and basic tests for moisture and ash content, in addition to tests for known adulterants and contaminants, and for pathogenic microbial bacteria, pesticides, residues and heavy metals,” he advised. “These monographs form the basis of our internal specifications, which inform what our purchasers can buy and how our QC unit will test and release ingredients for further processing,” he explained. “There is no shortage of test methods available; if a company is not following these tests and procedures, they are remiss in their QC responsibilities, because the standards and methods for most species are out there.”

A common QC process in high quality companies is refusing raw materials from any supplier who cannot demonstrate the botanicals passed tests based on any of these standards. For some suppliers, this often means using an independent lab, if there is no in-house lab to perform the tests. The company receiving the material also performs the tests for their own verification and QC satisfaction.

Despite the availability of monographs and standards, companies and botanical trade associations have had to develop and validate tests for various reasons, including the arrival of new herbs to the market. Perhaps 10 years ago, such information on standards and methods for certain botanicals was harder to come by, and companies had to develop and validate their own tests, often working with independent labs, but the need to develop standards in-house has waned. That said, newly popular exotic herbs can require testing development. One of the American Herbal Products Association’s (AHPA) most recent testing standards projects focused on hoodia, which became hugely popular shortly after hitting the market. Another reason would be if a company produces a unique herbal formula, combining a number of extracts with different matrices, which could interfere with analysis based only on methods for each individual botanical. In these cases, it is often necessary to modify or expand the official method or monograph to suit the combination, using various labs to validate and ensure reproducibility of results.



## Making Quality the Standard

When talking botanical manufacturing and quality, the words “standards” and “standardization” are heavily employed. By strict definition, the standards are the rules, and standardization is the process. However, the working definition of standardization in the marketplace has been confusing. Mark Blumenthal, founder and executive director of American Botanical Council (ABC), outlined the confusion: “For some, standardized means a product is manufactured to ensure that a given marker compound(s) meets a specified level. To others, it is a consistent manufacturing process. For still others, it is a specified ratio of herb material to solvent or a specified amount of herb in a dosage unit. In its broadest (and increasingly popular) sense, standardization refers to the control and manipulation of every aspect of the agricultural and manufacturing process, and beyond, to ensure a consistent product.” (*Herbalgram*. 2001;52:25).

Blumenthal explained standardization broadly refers to control and management of the agricultural and manufacturing processes, and can extend to cover industry-wide established common herbal names, safety labeling and validated analytical methods for herbal products. He confirmed the biggest debate surfaces over the labeling of “standardized” botanical products.

“What standardization really is and what it is marketed as might not be the same thing,” cautioned Michael McGuffin, president of AHPA, who called the period spanning the late ’80s and early ’90s a “decade of confusion” on what standardization means. Spelled out in its 2003 white paper on standardization of botanical products, AHPA’s definition of standardization is “the complete body of information and controls that serves to optimize batch-to-batch consistency of botanical products.” To AHPA and other longtime herbal insiders, the idea of standardizing to a strict percentage of specific marker compound(s) is merely a subset of standardization as it relates to QC and the manufacturing process.

Brinckmann agreed companies can make standardized products in many ways, not just in fixing levels of chemical marker compounds. “You can argue traditional preparations made the exact same way for hundreds of years benefit from a standardized methodology, including plant selection, identification, efficacy testing and manufacturing protocol,” he stated. He added the idea of standardization can be oversimplified. “Merely guaranteeing a minimum or maximum level of a particular chemical marker is not enough to ensure quality,” he warned. “There still could be wide variation of everything else in the matrix that wasn’t subjected to standardization. There are hundreds of chemicals in plants, and when standardizing to one or two phytochemicals, the other 98 or 200 could be in different ratios than in nature.” He further noted harvesting plants at the right time and having quality people analyze the materials and make determinations will result in a remarkably standardized product batch-to-batch, whether fixing the extract to a chemical marker or not.

So why standardize to specific chemical content? Cal Bewicke, president of Ethical Naturals, explained the early days of herbal products in America featured tablets or encapsulated powders comprised only of leaves and roots of herbs. Some were sold as extracts, powdered or liquid, but there was no way to determine if ratios given for active compounds were accurate. As more advanced analytical equipment methods became available, the in-depth technical analysis of the chemistry and activity of medicinal and therapeutic herbs became more widespread.

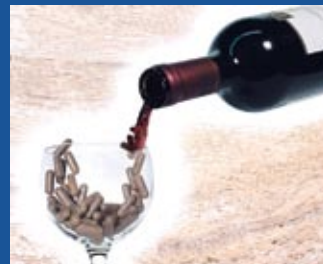
According to Bewicke, much of the original work was done in Europe: “A good example of this is the work done with ginkgo extracts by Schwabe, a German company. They identified the benefits of ginkgo for maintaining mental acuity into old age, and also identified a group of compounds (ginkgo flavone glycosides) that could be measured in the extract. Thus, they were able to perform clinical trials with a highly concentrated ‘standardized’ extract, which could then be reproduced for commercial use.” In fact, he said ginkgo was probably the first standardized extract imported and widely marketed in the United States. Other extracts followed—including saw palmetto, milk thistle, ginseng, valerian and echinacea—and industry groups such as AHPA and various labs formalized testing standards for these herbs. “Soon a wide range of such extracts were available, with standards that were relatively easy to test by HPLC or other methods,” Bewicke noted. “There is no doubt standardization greatly increased the quality and availability of herbal products on the market.”

Jack Klein, co-founder of JaW Associates, summed up the original intent of standardization. “It is appropriate if the actives are known and proven scientifically for a certain benefit; otherwise standardizing to markers is simply a way to ensure the correct herb and species,” he said. “It wasn’t that standardizing meant the extract was more efficacious—many herbal products are not standardized but are efficacious.”

However, Bewicke and McGuffin both noted the emergence of standardizing to specific marker compounds, and opening up the tests for these, has created an opportunity for

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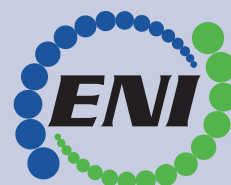


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unscrupulous parties to manipulate tests and fool buyers by adding cheap alternatives that mimic compounds during testing. Such economic adulteration has become quite ubiquitous. For example, with Panax ginseng, the root is widely considered the root of the herb's therapeutic activity; however, large quantities of the leaf can be added to surreptitiously increase levels of ginsenosides, a typical standardization marker for ginseng. In the case of pomegranate, ellagic acid can be added to the pomegranate extract to fraudulently meet the guaranteed amount in the final extract without spending the money on more dry material.

Other common products of economic adulteration focus on flavonoids and caffeine. Cheap flavonoids, a common plant phytochemical group, can be added to extracts such as ginkgo and grape seed extract. In the case of ginkgo, much of the clinical work has focused on the 24/6 extract—24 percent flavone glycosides and 6 percent terpine lactones. Spikers use cheap flavonoids to meet the 24 percent flavone requirement.

Klein said one of the flavonoids in the ratio is easily duplicated: "It isn't hard for cheaters to get the six flavonoids that comprise the 24 percent, but there is a unique ratio between those six flavonoids that only the right ginkgo will show in testing."

Bilberry is another botanical extract ripe for economic adulteration. Ed Croom, Ph.D., botanist and scientific and regulatory affairs manager with Indena, noted bilberry is standardized to anthocyanoside content (25 percent), which can be manipulated by blending in cheaper berries, such as black currant and elderberries; reports show even amaranth has been used to spike bilberry (*J Agric Food Chem*. 2006 Sep 20;54(19):7378-82). "Economic adulteration is an evolving problem, and staying on top of adulterants is an ongoing process," Croom said.

Another, less salacious source of adulteration is misidentification of a species, resulting in the wrong plant being extracted or brought to market. For this reason, Greg Ris, vice president of sales, Indena, advised, before standardization of any kind can begin, the starting material is important. "You have to respect good agriculture collection practices (GAPs)," he said, noting identification of species is an early necessity that should be part of a high quality company's know-how.

Croom advised identification of correct species and part are most easily done at the time of cultivation or collection of the plant material. He said tests in this area of QC are based on appearance, morphology (form and structure of plants) and classical taxonomy (technique of classification). "For plant identification relative to GMPs, there must be traceability back to cultivation," he said. "Basically, you ensure the material is what you want it to be and what the supplier says it is, using a quality management system; all of this is done well before you make an extract or powder."

Croom said misidentification, which has led to a number of wrong and dangerous materials on the market, can often be prevented with simple, non-chemical applications. "In the infamous digitalis-plantain controversy, it was reportedly a mix-up, and no one knew how to test for the digitalis/foxtail," he noted. "Now it is easy to test for it: looking at the hairs on digitalis and on plantain using anatomic microscopy will show you the difference between the two plants."

This is where knowing the agricultural source of the material is vital, according to Croom, who said knowing a similar-looking plant is growing near or around the intended plant is an unmistakable red flag. This should prompt a company to seek out or create a way to test for that possible contaminant. For example, he noted there is one species of St. John's wort used in humans, but over 300 wild species of the herb have not been researched for human benefit. If the whole field is not correctly identified as the one right species for humans, the wrong species could pass through many people, such as brokers, who do not know the origin of the material.

Highlighting how simple the identification could be, McGuffin noted one company in the digitalis-plantain debacle rejected the misidentified batch using non-chemical analysis. He explained old fashioned Frontier Natural Products, Norway, Iowa, had a human being who was responsible for visually and organoleptically identifying incoming material. When this person received the digitalis-containing "plantain" shipment, the strange color and odor didn't pass the test, and the material was rejected. McGuffin said this demonstrates companies need to employ every QC tool available, technological or not.

To test for adulterants, whether based on economic fraud or misidentification, QC has to know for what substance to test. "Fortunately, medicinal plants are a thousand-year-old trade, and a lot of the tricks of adulteration are well known," Brinckmann said. In the cases of innovative or newer adulterants, the response from industry and test developers is crucial to turning a negative into a positive.

Beyond adulteration, the desired finished product, whether a standardized extract or not, can start to inform commerce or agriculture and collection. Farmers begin to select varieties based on demand from buyers, sometimes culling out varieties that don't have high levels of desired marker compounds. This can happen in different directions. Sometimes farmers select plants with high levels of compounds that, when isolated, can be toxic to humans. However, pollinators such as bees might need those compounds—as with the alkaloids in comfrey, coltsfoot or borage—and the absence of these alkaloids could cause a whole cavalcade of weird things to happen in nature. On the other side, as echinacea started to become standardized to phenolic content, science found out the leaf had higher phenolic content than the traditionally used flower tops; farmers therefore began to harvest crop pre-bloom for the leaves, to minimize biomass and end up with a more economic extract. In the end, harvesting is changed to maximize compounds that may or not be keys to therapeutic benefits.

Similarly, saw palmetto berries have traditionally been harvested when ripe. Some companies don't make extracts but grind the berries into powders for capsules and tablets. These companies found the oils in the ripe berries complicated the manufacturing process, so they influenced farmers to harvest green, unripe berries. This goes against traditional methods and ignores the majority of clinical research on saw palmetto, which indicates benefits from the fruit oil from ripe berries.

Saw palmetto has long been standardized to 85 percent fatty acids (FAs), if only for the reason the company that first brought the standardized extract to market did tests on that percentage of FA content. "I don't believe the other 15 percent of compounds are useless," McGuffin argued. "I also know there is a rich historical record of simple tincture—which contains nowhere near the 85 percent—having therapeutic benefits."

The bottom line is science has not yet figured out the active constituents in each of the hundreds of plants on the market, let alone determined whether there are one or two groups of compounds responsible for therapeutics or multiple compounds within the matrix. The key then is not standardization to markers alone, rather a manufacturing process standardized to ensure consistency from batch to batch, using established QC protocols and methods that are, for the most part, widely available. Quality does not come cheap, and looking for a bargain, which is the American way, invites QC problems. Brinckmann assured, "If you are understand QC costs and don't balk at the premium expense, these problems start to go away." □

Part two of this feature on botanical quality will appear in the 11/19 issue of *INSIDER*.

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