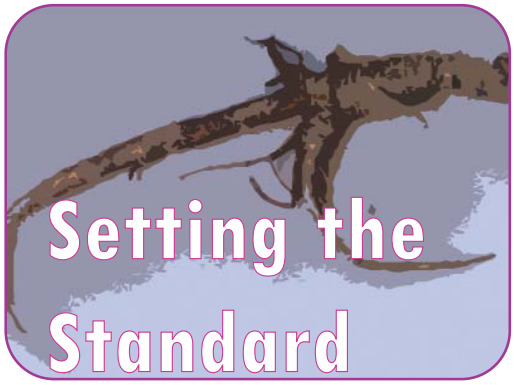

Setting the Standard

A Case Study in the Need for Herbal Standardization

If you want to start a brawl at an herbalist or naturopathic physicians' conference, bring up the issue of the *standardization* of botanicals. *Standardization* is the process of concentrating an herb so that one or more of its key phytochemicals or other ingredients is present in a defined ("standard") amount. (On the flip side, standardization can also involve ensuring that some ingredients are *not* present, or are kept below a maximum tolerable level; this might include toxic constituents of the crude herb, such as the *ginkgolic acids* in *Ginkgo biloba*).

The idea behind standardization is to ensure that each capsule contains a consistent amount of the key ingredients that give the herb its effects. That would seem to be an uncontroversial idea. We all know that soil, weather, and seed characteristics can cause wide variations in the amounts of vitamins and other nutrients in conventional food, and the same applies to the phytochemicals that give botanicals their unique healing powers. Standardization aims to ensure a reliable supplement by guaranteeing key ingredients are present in reliable, defined amounts.

But standardization is not without its critics, and many of them are passionate. Many more conservative herbalists, especially, argue that the effect of an herb cannot be pinned down to specific, individual ingredients, but is the result of the synergistic interactions of the whole. In this view, efforts to standardize herbs may actually be counterproductive, as the process of concentrating a few *specific* constituents may *reduce* the levels of these other, less-understood ingredients, or upset the balance of the various constituents found in the crude herb. Some even believe in a kind of "life force" present in whole, unconcentrated herbs, which is "killed" by the process of concentration and extraction.

It must be said, right from the start, that the most rigorous scientific evidence to support the health-giving powers of herbs comes from high-quality clinical trials performed under the sponsorship of European "phytopharmaceutical" companies, using their carefully-researched precision processes for herbal standardization. There are rigorous studies that prove the effectiveness of ***Rhodiola rosea*** in improving performance under stressful conditions,[1-3] and the ability of defined pollen extract (*not* bee pollen!) to not only treat the *symptoms* of **benign prostatic hypertrophy (BPH)**, but to actually reduce prostate *volume*[4-7] (unlike saw palmetto, which reduces the symptoms of BPH but does not affect the volume of the prostate itself[8,9]).

But this evidence comes from controlled trials performed using *standardized* botanical supplements, whose carefully-defined extraction procedures are designed to ensure that every batch contains a reliable dose of its key active ingredients. These trials prove that these standardized extracts work; they don't demonstrate that the plain herb, as it comes out of the dirt, will work in the same way – or that they will work *reliably* or *consistently*. Normally, the only evidence for crude herbs comes from *folklore* – not randomized, double-blind, controlled trials.

Still, some would argue that the fact that most raw herbs have not been tested as scientifically as standardized extracts doesn't prove that they don't work. And advocates

for such herbs tend to insist on the importance of unknown, synergistic components almost as an article of faith, even in the absence of any evidence on the subject, one way or the other. So concrete examples of the importance of standardization are important to settle the issue.

One case study in the need for standardization to ensure an herb's effectiveness that has just recently come to light is in **the use of American ginseng (*Panax quinquefolius* L.) to reduce "postprandial glucose excursions"** – the jump in blood sugar levels that happens in the two hours following a meal. Postprandial glucose is shaping up to be a major issue in long-term health – especially for people suffering with **diabetes**, but also for the rest of us. Evidence is mounting that, even in people with "normal" fasting glucose readings, **postprandial glucose is more strongly associated with risk of developing diabetes, cardiovascular disease, and diabetic complications than are either fasting blood sugar levels or HbA1c.**[10-12]

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There are probably several reasons for this higher risk, mostly connected with the formation of *Advanced Glycation Endproducts (AGEs,* which are discussed elsewhere in this issue of *Advances*). Beyond the obvious fact that the higher blood sugar levels that follow a meal provide more opportunities for the formation of **Schiff's bases** (early, but still reversible, products of the reactions between sugars and proteins), the high blood sugar levels that occur after a meal also prevent *existing* Schiff's bases from reversing themselves, increasing the risk that they will go on to form full-blown AGE.[13] Additionally, the postprandial period causes a surge in **oxoaldehydes** (the highly reactive, AGE-forming compounds formed during the metabolism of glucose, or as a result of the oxidative breakdown of sugar polymers or of intermediates in AGE chemistry),[14] further accelerating the AGEing process.

This means that anything you can do to keep postprandial glucose under control is a key to preventing AGE formation and preserving your long-term health. So when a team of Canadian researchers published, in rapid succession, a series of groundbreaking studies showing that American ginseng lowers postprandial glucose levels in both diabetics[15,16] and people with "normal" glucose levels,[17,18] excitement built up quickly. The importance of their findings was reinforced by a longer-term study which showed that regular American ginseng supplementation led to better *overall* glycemic control, as measured by fasting glucose and HbA1c.[19] It seemed that a major step forward had been made in protecting the health of diabetics and healthy folks alike, using a safe, inexpensive dietary supplement.

Unfortunately, these hopes were dashed – or, at least, pushed out of immediate grasp – when a new study, carried out by the same research group using a similar protocol, found **no effect on postprandial glucose from American ginseng supplement use.**[20]

Exactly what caused this flop, after a string of successes, is not yet known with certainty – but the basic nature of the problem is clear. *All* of the trials had been performed using unprocessed American ginseng root harvested in Ontario, provided to the Canadian research team by the same supplier. But all of the *successful* trials had been performed using *one* crop – while the later, failed trial used another.[20] As with all plants, each crop is different – and *something,* clearly, was different enough between the two batches of American ginseng to lead to a series of successes with the first batch[15-19] and a complete failure with the later one.[20]

The researchers *had* analyzed the original batch of American ginseng, and characterized its unusual profile of **ginsenosides** (the phytochemicals to which conventional *Panax ginseng* is normally standardized for its adaptogenic use).[18] But **the active ingredients in this American ginseng had not been identified, and the supplement was not standardized.** They had not identified *what it was*, exactly, about this botanical that gave it its glucose-lowering powers – so they were in no position to ensure that a given batch of American ginseng would deliver a reliable dose of its key active ingredients.

One difference between the two crops was in their *total* ginsenoside content: the failed batch contained only half as much ginsenoside as the original crop. But doubling the dose of ginseng from the new batch (to bring the users' total ginsenoside intake up to the level in the original trials) still led to a flop.[20] A more likely explanation is the *ratio* of *specific* ginsenosides: the blend of the failed batch had a much higher percentage of **propanaxatriols** in it than the original crop, and previous studies suggest that propanaxatriols may actually *inhibit* the uptake of blood sugar by cells.[21,22]

As things stand, batch-to-batch variations in whole, unprocessed American ginseng root make a crap shoot out of its potential use to lower your postprandial glucose spikes. Until the true active ingredients are identified and standardized – and any possible *opposing, counterproductive* ingredients minimized on a reliable basis – there will be no way to know whether a given American ginseng pill will save you from damage to your retinas, nerves, and kidneys – or wind up being a waste of money, or even *harmful* to your overall blood glucose balance. Even if you were to buy a bottle of American ginseng and *verify* that it works by testing your glucose levels after a meal, that would be no guarantee that the *next* bottle you bought would work as well – even if it comes from the same supplier, or even the same farm!

There are certainly other examples of this problem. We now know that the *hypericin* to which most St. John's Wort is standardized is at best an indirect marker of its effectiveness,[23] and that *hyperforin* is the true active ingredient and the proper basis for standardization.[24] Because hyperforin is known to be unstable,[25] any non-standardized, crude St. John's Wort herb or oil extract sitting on a health food store shelf will almost certainly be lacking in this key phytochemical, no matter how rich in hyperforin the original flowering tops of the living herb may have been.

The active ingredients in this American ginseng had not been identified, and the supplement was not standardized.

Still other examples are lurking in the private files of the European phytopharmaceutical companies that spearheaded the original research into the herb in question; it's just this kind of research which underlies the standards for the processing of the crude herbs into the effective, reliable, clinically-tested botanical extracts and concentrates, and which has made European herbal medicine a true science, instead of a mixture of guesswork and word-of-mouth. The bottom line: without standardization, there is no way to know just what a given herbal supplement can deliver. And while you may just have to live with the fact that some of the oranges on the produce shelf contain just a fraction of the average 60 milligrams of vitamin C, there is no good reason why you should accept the same unreliability from your *Bacopa* supplement.

Herbal medicine may deliver "miracle cures," but these health benefits come from the botanicals' *biochemistry* – not from any mystical, untestable "healing force." Like everything else in the living world, herbs are biological "factories" for a host of naturally-synthesized chemicals; *which* phytochemicals they produce, and *how much,* is the result of interactions between each plant's unique genetic inheritance and the conditions of its environment. In turn, their effectiveness relies upon the ability of these phytochemicals to modulate your internal biochemical balance. These herbs' key ingredients (or reliable secondary markers for their presence) must be identified, and supplements must be standardized in accordance with the best available science, if they are to be reliable. Putting herbs with unknown levels of key active constituents into your body – those that heal, and those that harm – is a *gamble*. And you're betting with your health.

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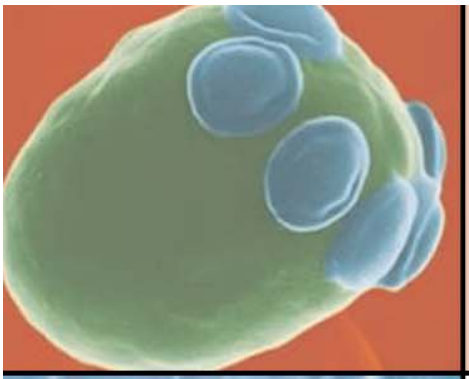

In Vino Vivo?

RESVERINS

***Trans*-Resveratrol** is a phytochemical found naturally in red wines. Many researchers think that the small amount of *trans*-resveratrol is responsible for the remarkable good health of the French. And now new research from the Harvard Medical School suggests that, at a slightly higher dose, it may be the key to much more.

Sirtuins are enzymes that guard the integrity of the DNA code, and regulate proteins central to cell repair and survival. The Harvard researchers call them the "longevity regulators" and "guardians of the human cell." Sirtiuns may be the key to the dramatic anti-aging action of **caloric restriction** – the only *proven* way to extend maximum lifespan in mammals.

A study has revealed that *trans*-resveratrol is a "**Sirtuin Activating Compound**," cranking up the activity of these protective proteins. Given the right dose, unicellular *S. cerevisiae* lives 80% longer. Human cells survive chemical and radiological assault. And researchers say their work in flatworms and fruitflies – humble, but multicellular – looks promising.

Resverins from AOR delivers 20 milligrams of *trans*-resveratrol in each vegetarian capsule.