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August 2014 US$39.00

SPECIAL REPORT

A Closer Look at Phytonutrients

Phytonutrients are becoming an important feature in product development as consumer interest increases in plant-based foods. As researchers uncover the benefits of phytonutrients, the key is to get enough of these nutrients to make a meaningful health impact, as well as to ensure they are consumed in a healthy balance, similar to that in whole foods.

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SPECIAL REPORT

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Phytonutrients Moving Closer to Mainstream Product Development

By Rachel Cheatham, Ph.D.
Contributing Editor

There was a day when the term antioxidant was unfamiliar to consumers. Today, antioxidant is arguably squarely placed in everyday terminology for the health-conscious consumer. While the scientific term "phytochemical" and the more consumer-friendly term "phytonutrient" are still making headway into commonplace understanding, there is no doubt consumer demand and interest in all things plant-based is here.

"The consumer is not yet familiar with the word 'phytonutrient,' perhaps, but they are very familiar with the idea that plant-based foods have inherent nutritional value beyond the basic vitamins and minerals," said Connie Diekman, ME.d, RD, LD, FADA, director of university nutrition, Washington University, Saint Louis. "And anything linked to better health is in demand."

Leaning Toward Phytonutrients

Consumers are actively recognizing that all those fruits, vegetables, nuts and seeds must contain some sort of nutrients that confer health benefits beyond the basic standbys like vitamins A or C. Think back to those television commercials a few years ago in which Alton Brown of Food Network fame talked about anthocyanidins to the American public on behalf of Welch's grape juice. It was an early sign of the changing phytonutrient times.

Much of the consumer attention on plant-based compounds is ultimately born out of the known harms of oxidation in the body as a result of various stressors ranging from environmental to psychological. These stressors led to an ongoing fervor around anything that could essentially antioxidize in the body. Such high interest also sparked a scoring mechanism known as oxygen radical absorbance capacity (ORAC), which was based on a simple in vitro assay done in a test tube. ORAC caused many marketers to latch onto quantifiable antioxidant levels used in various marketing angles and claims with consumers.

"The issue is many brands don't necessarily realize that the USDA pulled the ORAC database in an effort to curtail questionable claims tied to the validity and appropriateness of the scoring system for product marketing," Diekman said. "The reality is there is a lag between scientific and policy developments on one hand and product marketing and the consumer on the other. Through it all, the health-conscious consumer is still looking for their hit of antioxidants."

According to the International Food Information Council (IFIC) Foundation, nearly 90 percent of Americans say they are interested in learning about foods that have health benefits beyond basic nutrition, which can include functional foods that contain phytonutrients. In addition, data also finds 63 percent believe such functional foods will improve health if consumed regularly. The other data finding, not surprisingly, is that taste rules when it comes to food choice, which is a particularly interesting challenge in the phytonutrient space.

"Phytonutrients are the very nutrients in the plant designed to protect the plant from disease and predators. They are often quite unpleasant in taste because they are often toxic by design," said Adam Drewnowski, Ph.D., professor of epidemiology and director of the Center for Public Health Nutrition at the University of Washington, Seattle.

> Epidemiological evidence routinely points to the benefits of fruits and vegetables.

Phytonutrients are almost always bitter, acrid or astringent. Although often quite beneficial to human health in relatively small doses, many phytonutrients are technically toxic. In fact, many of the bioactive phytonutrients being rigorously studied in laboratories across the globe have been previously treated by industry and consumers alike as waste, or at least not edible. As a point of reference, think how the nutrient-dense kale leaf was once reserved for garnish not consumption, and now it's the hottest leafy green on the market in everything from green juices to kale chips. In addition to extremely high levels of vitamins A, C and K, kale contains more than 45 different flavonoids and glucosinolates.

Breaking Down the Phytonutrient Categories

Epidemiological evidence routinely points to the benefits of fruits and vegetables. A recent meta- analysis appearing in *The BMJ* pooled data from 16 prospective cohort studies and concluded higher consumption of fruit and vegetables was significantly associated with a lower risk of all-cause mortality. There still exists much debate around the dose response relationship between how many servings of which fruits and vegetables are needed to positively impact health. The other issue is the evolving understanding of what specific compounds in which fruits and/or vegetables confer a specific health benefit on the individual level. It is a very large matrix of knowns, unknowns and possibilities.

Estimates of the number of phytonutrients that exist—both discovered and undiscovered—range anywhere from 4,000 to more than 25,000 compounds. The wide range is indicative of the fact that many of these nutrients have yet to be identified, let alone fully characterized in their chemistry and mechanism(s)

of action. Broad categories have emerged that typically get grouped into three main areas:

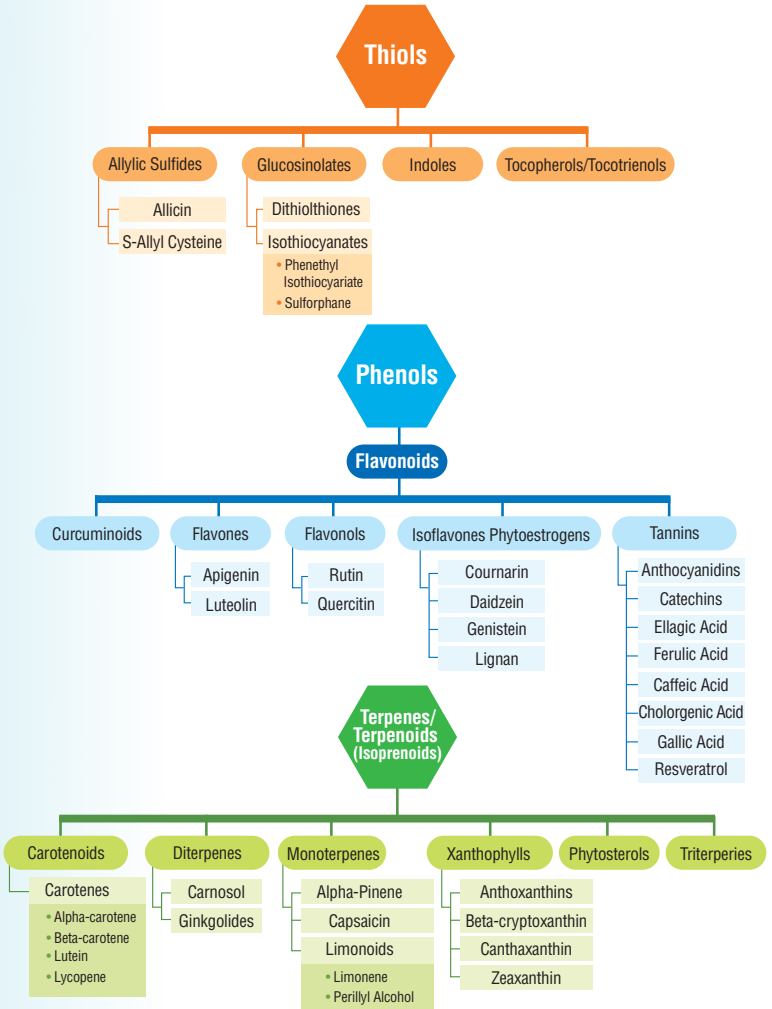
Thiols-Sulfur-containing compounds such as glucosinolates, which include isothiocyanates as a subset.

Phenols-Includes the broad category of flavonoids with tannins and isoflavones as subsets.

Terpenes-Includes the broad category of carotenoids with alpha-carotene, beta-carotene, lutein and lycopene as subsets.

Consider as an example the isothiocyanates, which are found at high levels in cruciferous vegetables such as broccoli. They are the breakdown product of glucosinolates and are sulfur-containing compounds thought to protect against cancer, because they help eliminate carcinogens from the body and enhance

Types of Phytochemicals



Thiols

Chemically, a type of mercaptan with a sulfhydryl functional group, often found in *Allium*. Can protect cells from oxidative damage.

Phenols

Also called phenolics, have a hydroxyl group (—OH) bonded directly to an aromatic hydrocarbon group. Phenols protect against oxidative damage and inflammation.

Terpenes/Terpenoids (Isoprenoids)

Hydrocarbons consisting of isoprene units (molecular formula C_5H_8) found in a wide variety of plants. Their functionality depends on their structure, but may provide anti-cancer and cardiovascular-health properties.

the transcription of tumor-suppressor proteins. Glucosinolates are found in relatively high concentrations in commonly consumed portions of cruciferous vegetables. A half-cup serving of raw broccoli is thought to provide more than 25 mg of glucosinolates, for example.

When it comes to broccoli consumption, over 90 percent of the broccoli eaten in the United States is grown in California, but this makes it costly to distribute to the East Coast, plus phytonutrient potency and freshness diminishes with excessive shipping time. A project to address such issues called the Eastern Broccoli Project has been in progress with the hope to not only extend broccoli's growing season through conventional-breeding methods, but also to investigate phytonutrient density in relation to growing methods.

A half-cup serving of raw broccoli may provide more than **25 mg** **of glucosinolates.**

"Our work on this sort of project, and in general, is to focus on improving the phytonutrient content of the plant itself. Agriculturally speaking, if we can offer plants with higher phytonutrient densities that consumers still enjoy the fresh taste of, then we have a true winner when it comes to better health through diet," said Carl Sams, Ph.D., professor of plant sciences, University of Tennessee, Knoxville.

Drewnowski commented, "The debittering of plant foods has been a long-standing sensory concern for food scientists." He added new plant cultivars could theoretically be made less, not more, nutritious in well-intentioned attempts to dampen any bitter notes. Working at the intersection of agriculture and nutrition science will be critical. Specific cultivars, which have relatively higher levels of naturally occurring sugars, could be selected as a way to help keep bitterness in check, while at the same time maintaining phytonutrient potency.

"Of course, adding a little salt, butter or cream never hurt either," chuckled Drewnowski.

Coming Full Circle

Some 20 years ago, during the health-nut era, there was strong industry interest and emphasis on standardized extracts to create healthier foods.

"The industry was struggling to find standardization methods as to how to test for different marker compounds to ensure a known percent of the desired bioactive was present. Now leap forward two decades, and we are getting a steady stream of requests for essentially standardized whole foods-based ingredients. The main thing that has changed is moving from extract to whole foods-based ingredients," said Ginny Bank, research and development lead at RFI, Blauvelt, New York.

While there is a lack of regulatory definition around concepts like "whole-food extracts" or "whole-food ingredients," the consumer demand for food products that contain some portion of an intact component of a food, particularly one with a high phytonutrient value, is rapidly increasing as consumers seek less-processed foods. A lack of clear definition in this area does not equate to a lack of indirect demand; that is, the average consumer may not follow the details around extracts, flavors or concentrates, but when they see recognizable whole-foods-based ingredients listed on the label, like carrots or cranberries, they will no doubt view this product as healthier, regardless of the level of processing.

One such ingredient that is trending upward is black garlic, a type of garlic produced through fermentation methods. Black garlic is a sweet and tangy paste that is high in a compound known as S-allycysteine, which is a water-soluble organosulfur compound that would fall under the broader thiol category of phytonutrients. Garlic-derived organosulfur compounds have been found to inhibit the activity of the inflammatory enzymes, cyclooxygenase and lipoxygenase. The specific health benefits associated with aged or fermented versus raw garlic are less well-characterized. Nonetheless, the rising interest in black garlic is largely born out of the phytonutrient plant-based trend combined with the concurrent fermented-foods trend.

The Evolving 'Whole Foods' Food Supply

Currently, most Americans get their phytonutrients from a limited number of foods. In fact, research suggests that for five phytonutrients, in particular alpha-carotene, beta-cryptoxanthin, lycopene, hesperetin and ellagic acid, a single food accounts for 64 percent or more of the total intake of that phytonutrient in the diet. The data analysis looked at nine phytonutrients: α- and β-carotene, β-cryptoxanthin, lutein/zeaxanthin, lycopene, anthocyanidins, hesperetin, quercetin, and ellagic acid. It found that tomatoes, carrots, oranges and orange juice, and strawberries accounted for approximately two-thirds or more of the average intake of five out of the nine phytonutrients. Carrots, spinach and onions each contributed between 26 percent and 31 percent to intakes of three of the remaining compounds. For example, 81 percent of lycopene intake among Americans comes from tomatoes. (*Journal of the Academy of Nutrition and Dietetics*. 2012;112:222-229).

> The question becomes, how do we help consumers eat enough of these important plant-based nutrients to make a meaningful health impact?

The question becomes, how do we help consumers eat enough of these important plant-based nutrients to make a meaningful health impact? To date, many of the sources swing either between completely whole fruits and vegetables on one side or dietary supplements on the other, without much middle ground.

Eating whole foods is certainly sound advice; however, consumers also demand convenience, portability and affordability, all of which can sometimes run counter to eating whole foods at every meal and snack. On the other hand, dietary supplements can offer a viable alternative to shore up nutrient shortfalls, but questions remain on the best delivery mechanisms for phytonutrients.

"We have the technical skills to isolate, extract and assay the phytonutrients of greatest health interest. But once that phytonutrient is pulled out of the original food matrix, it can behave in different and unexpected ways. The phytonutrient bioactivity may rely on the presence of five other compounds in the original plant, and we simply don't yet understand all those complexities," Sams said.

Meanwhile, as the industry continues to figure out how to best incorporate whole food ingredients into various processed and packaged foods, the juice world soars. Gone are the days of choosing between orange or grape juice. In fact, orange juice sales hit a record low with sales down over 8 percent since last year. Such a finding is likely less about consumers not liking orange juice anymore, and more about consumers seeking the latest and greatest "super fruit" of the day. From tart cherry and pomegranate juice to açaí and Muscadine, consumers are increasingly sophisticated about their juice choices. The key, nutritionally speaking, is that the juice is 100 percent juice, which means no added sugars.

Juice comprised of Montmorency cherries, for instance, has been shown to help with muscle recovery in endurance athletes by helping attenuate oxidative and inflammatory responses. As part of the study design, athletes were given a dose of "MC equivalent," (reported to contain 9.117 mg/ml of anthocyanins) equal to approximately 90 whole Montmorency tart cherries, twice daily. While this and related research continually points to the undeniable power of phytonutrients, it is also a good example of where the end consumer would likely not be able to consume the whole foods version at levels deemed efficacious. In turn, phytonutrient delivery forms beyond pure whole foods, like juices, bars, chips or supplements, are becoming a necessary and worthy path for future product development.

"Just don't jump the gun and don't make claims that aren't supported by volumes of research," Diekman said. "That's the big one. But make no mistake, phytonutrients are here to stay. Product developers that crack the phyto code will be rewarded." ❑

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Antioxidants and Cancer: Proceed with Caution

By Lynn A. Kuntz
Executive Editor

It's been well-established that oxidative stress and the production of free radicals in the body is linked to aging, cancer and certain other diseases, hence the popularity of dietary antioxidants, plant-based or otherwise. This has led to research that has investigated the relationship between dietary antioxidant supplements and reduced risk of cancer in humans.

According to the National Cancer Institute (NCI) at the National Institutes of Health (NIH), Bethesda, Maryland, many observational studies have been conducted that look at the relationship between dietary antioxidant supplements and reduced risk of cancer in humans, but that "overall, these studies have yielded mixed results." Plus, they may have biases that limit their reliability.

Randomized, controlled clinical trials, however, provide better evidence of any nutrient/health relationship. The NCI notes that, to date, nine of these trials on antioxidants such as beta-carotene, and vitamins A, C, and E (alpha-tocopherol) and selenium (all in supplement form) for cancer prevention have been conducted worldwide:

Linxian General Population Nutrition Intervention Trial

- "Nutrition intervention trials in Linxian, China: supplementation with specific vitamin/mineral combinations, cancer incidence, and disease-specific mortality in the general population." *Journal of the National Cancer Institute* 1993;85:1483-91
- "Total and cancer mortality after supplementation with vitamins and minerals: follow-up of the Linxian General Population Nutrition Intervention Trial." *Journal of the National Cancer Institute* 2009;101(7):507-518.

Alpha-Tocopherol/Beta-Carotene Cancer Prevention Study (ATBC)

- "The effects of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers." *New England Journal of Medicine* 1994;330:1029-35.
- "The effects of supplementation with alpha-tocopherol and beta-carotene on the incidence and mortality of carcinoma of the pancreas in a randomized, controlled trial." *Cancer* 1999; 86(1):37-42.

- "Effects of supplemental alpha-tocopherol and beta-carotene on urinary tract cancer: incidence and mortality in a controlled trial (Finland)." *Cancer Causes and Control* 2000;11(10):933-939.
- "Effects of supplemental alpha-tocopherol and beta-carotene on colorectal cancer results from a controlled trial (Finland)." *Cancer Causes and Control* 2000; 11(3):197-205.
- "Effects of alpha-tocopherol and beta-carotene supplementation on upper aerodigestive tract cancers in a large, randomized controlled trial." *Cancer* 2007; 109(5):891-898.

Carotene and Retinol Efficacy Trial (CARET)

- "Effects of a combination of beta carotene and vitamin A on lung cancer and cardiovascular disease." *New England Journal of Medicine* 1996;334(18):1150-1155.
- "The Beta-Carotene and Retinol Efficacy Trial: incidence of lung cancer and cardiovascular disease mortality during 6-year follow-up after stopping beta-carotene and retinol supplements." *Journal of the National Cancer Institute* 2004;96(23):1743-1750.
- "Dietary supplement use and prostate cancer risk in the Carotene and Retinol Efficacy Trial." Cancer *Epidemiology, Biomarkers & Prevention* 2009;18(8):2202-2206.

Physicians' Health Study I (PHS I)

- "Lack of effect of long-term supplementation with beta carotene on the incidence of malignant neoplasms and cardiovascular disease." *New England Journal of Medicine* 1996;334:1145-9.

Women's Health Study (WHS)

- "Beta-carotene supplementation and incidence of cancer and cardiovascular disease: Women's Health Study." *Journal of the National Cancer Institute* 1999;91:2102-6.
- "Vitamin E in the primary prevention of cardiovascular disease and cancer: the Women's Health Study: a randomized controlled trial." *JAMA* 2005; 294(1):56-65.

Supplémentation en Vitamines et Minéraux Antioxydants (SU.VI.MAX) Study:

- "The SU.VI.MAX Study: a randomized, placebo-controlled trial of the health effects of antioxidant vitamins and minerals." *Archives of Internal Medicine* 2004;164(21):2335-2342.

- "Antioxidant supplementation increases the risk of skin cancers in women but not in men." *Journal of Nutrition* 2007;137(9):2098-2105.
- "Incidence of cancers, ischemic cardiovascular diseases and mortality during 5-year follow-up after stopping antioxidant vitamins and minerals supplements: a postintervention follow-up in the SU.VI.MAX Study." *International Journal of Cancer* 2010;127(8):1875-1881.
- "Incidence of skin cancers during 5-year follow-up after stopping antioxidant vitamins and mineral supplementation." *European Journal of Cancer* 2010;46(18):3316-3322.

Heart Outcomes Prevention Evaluation—The Ongoing Outcomes (HOPE-TOO) Study:

- "Effects of long-term vitamin E supplementation on cardiovascular events and cancer: a randomized controlled trial." *JAMA* 2005;293(11):1338-1347.

Selenium and Vitamin E Cancer Prevention Trial (SELECT):

- "Effect of selenium and vitamin E on risk of prostate cancer and other cancers: the Selenium and Vitamin E Cancer Prevention Trial (SELECT)." *JAMA* 2009;301(1):39-51.
- "Vitamin E and the risk of prostate cancer: the Selenium and Vitamin E Cancer Prevention Trial (SELECT)." *JAMA* 2011;306(14):1549-1556.
- "Vitamins E and C in the prevention of prostate and total cancer in men: the Physicians' Health Study II randomized controlled trial." *JAMA* 2009;301(1):52-62.

The NCI has concluded that "Overall, these nine randomized controlled clinical trials did not provide evidence that dietary antioxidant supplements are beneficial in primary cancer prevention." To many, the CARET study was particularly alarming—so much so that researchers halted the study two years earlier than planned when they found that beta-carotene/retinol supplementation was associated with increased lung cancer and increased death from all causes. While the reason is unclear, some surmise that excessive levels of the antioxidants in the supplements actually aided free-radical formation.

According to the NCI, "the lack of benefit in clinical studies can be explained by differences in the effects of the tested antioxidants when they are consumed as purified chemicals as opposed to when they are consumed in foods, which contain complex mixtures of antioxidants, vitamins, and minerals. Therefore, acquiring a more complete understanding of the antioxidant content of individual foods, how the various antioxidants and other substances in foods interact with one another, and factors that influence the uptake and distribution of food-derived antioxidants in the body are active areas of ongoing cancer-prevention research."

All this data concludes that the push toward food-derived antioxidants and the panoply of phytochemicals they contain, might be a smart and effective move. ❑