

## Antioxidants are 'Pro'-Sales

By Sandy Almendarez, Managing Editor

Antioxidants is a pretty broad category. They appear in the form of vitamins (C and E), minerals (selenium, manganese and zinc), enzymes (superoxide dismutase [SOD], catalase [CAT] and glutathione peroxidase [GPx]), carotenoids (lutein, zeaxanthin and astaxanthin) and other nutrients such as coenzyme Q10 (CoQ10), polyphenols, uric acid and phytochemicals. Being found in all types of natural products, it makes sense antioxidants deliver abundant health benefits as well. The heart, skin, eyes, joints, brain and immune system are all said to benefit from antioxidants.

Antioxidants counter the damaging effects of oxidation. The body requires a balance of antioxidants and free radicals. If the body produces chemically active atoms or molecular fragments that have too many or too few electrons—free radicals—beyond its antioxidant capacity, oxidative stress occurs. Free radicals are highly unstable because of their unpaired electrons, and they scavenge the body looking to steal electrons from cells, proteins and DNA. This damages the cells in the body and can lead to disease. Because all cells can be damaged, antioxidants have many applications in the body. While it's impossible to avoid free radical damage, people have the ability to ingest antioxidants to help reduce the amount of oxidative stress within the body. The media, and consumers, have caught on to antioxidants' health benefits, which is furthering the demand for these ingredients.

"Consumer interest continues to rise sharply because people are now becoming more aware that 'antioxidants are good for me,'" said Dean Mosca, president, Proprietary Nutritionals Inc (PNI). "Thanks to tremendous boosts in mass-media coverage that focuses on fruits, berries and vegetables being stacked with these naturally occurring health promoters, a large number of consumers have made the connection."

Sharrann Simmons, marketing director North America, Cognis Nutrition & Health, said growth is driven by the expansion of the population that can be most helped by antioxidants. "Consumer interest is driven by a couple of factors," she said. "One is this whole phenomenon of the healthy aging Baby Boomer as antioxidants are useful for a lot of different problems associated with aging. Another driver is related: appearance."

Corey Jansen, associate product manager for the FloraGLO Lutein ingredient brand, Kemin Health, also said consumers want antioxidants, even if they don't know exactly what they do. "It appears there is more interest in antioxidants now from consumers than what there was three or four years ago," he said, adding, "However, in this industry, we assume consumers have a broad understanding of what antioxidants do, and sometimes the term gets overused so much consumers don't know what benefits they offer. Our challenge is to drill down to specifics, and teach consumers to look for proven ingredients, that have been used in clinical studies and shown to be effective and safe."

However, the days when an antioxidant claim alone would sell a product may be coming to a close, according to Brien Quirk, director of R&D, Draco Natural Products. "Consumer interest in antioxidants has leveled off compared to when the issue was newer. It seems to be more of a secondary feature of a nutritional supplement."

Still, as recently as 2008, antioxidant product sales were growing, as Ram Chaudhari, Ph.D., FACN, CNS, Fortitech, senior executive vice president and chief scientific officer, noted statistics published by Nutrition Business Journal show antioxidant supplements sales for 2008 totaled \$4.6 billion, up nearly 6 percent over the year before, and up from \$3 billion reported in 2006.

A naturally sourced antioxidant on the ingredient list may also help boost sales. "Consumers seem to be particularly interested in natural antioxidants from fruits for example," said Catherine Lecareux, marketing manager, Bio Serae Laboratoires.

Simmons noted the growing natural trend is backed by science. "It's well documented in a number of clinical studies that natural vitamin E is twice as bioavailable as synthetic, and there is major consumer demand for a natural-sourced nutrients versus synthetic."

## Science and Research

As stated earlier, health benefits of antioxidants are abundant, and thousands of clinical studies have been conducted on natural compounds considered antioxidants. These studies have linked diets rich in antioxidants to a lower risk for diseases including cancer, heart disease, stroke, cataracts, Parkinson's, Alzheimer's disease and arthritis.

The heart is a major benefactor to antioxidant consumption. "Antioxidants are important to protect low-density lipoprotein (LDL) cholesterol from oxidation," Quirk said. He added Draco's antioxidant formula D-40 is composed of several antioxidant- and polyphenol-rich herbs, including grape seed extract, rhodiola, schisandra, green tea and pine bark. In unpublished mice studies, D-40 reduced LDL cholesterol levels and increased the level of the body's SOD levels in red blood cells.

Sytrinol, supplied by PNI, is a blend of antioxidants, including polymethoxylated flavones (PMFs) and a range of palm tocotrienols. A 2007 study found daily treatment with Sytrinol significantly improved cardiovascular parameters compared to placebo with significant reductions shown in total cholesterol, LDL and triglycerides.<sup>1</sup>

Cyvex's signature product, BioVin®, is a full-spectrum grape extract made of red wine grapes. According to Matt Phillips, president of Cyvex, it is "a powerful antioxidant that scavenges free radicals, reducing oxidative damage to cells. It helps support resistance to oxidation, providing cardiovascular protection." A University of Toronto, Ontario, study found consumption of BioVin was associated with increased serum antioxidant potential and lower protein and LDL oxidation.<sup>2</sup>

Numerous other studies have found antioxidants from a variety of sources benefit the heart. For instance, subjects who received a blend of tocopherols for four weeks experienced a 10-percent decrease in cholesterol ( $P < 0.05$ ); while a group who received gamma-tocotrienol for four weeks experienced a 13-percent decrease in cholesterol levels ( $P < 0.05$ ).<sup>3</sup> Grape seed extract has been shown to protect against LDL oxidation,<sup>4</sup> and CoQ10 has shown positive results as an adjunct treatment to standard medical therapy in congestive heart failure.<sup>5</sup>

Antioxidant health benefits go well beyond the heart. Blueberries improve short-term memory,<sup>6</sup> cranberries prevent urinary tract infections (UTIs),<sup>7</sup> carotenoids benefit eye<sup>8</sup> and skin health,<sup>9</sup> and

supplementation with a combination of antioxidants (vitamins C and E, plus alpha-lipoic acid) and L-arginine supported nitric oxide (NO) activity and exercise performance in older athletes.<sup>10</sup> This sport benefit is behind Bio Sera's ViNitrox™, a blend of fruit extracts. "In vivo tests confirmed the potential of ViNitrox to reduce the harmful effect of peroxynitrites in stressful situations like sustained and repeated physical activity," Lecareux said. "In the experiment, two groups of hamsters (ViNitrox vs. placebo) were maintained under oxidative stress conditions. Plasmatic concentrations in nitrotyrosin (degradation products from oxidative stress) were significantly lower in the ViNitrox group ( $1.32 \pm 0.43$  nmol/l) compared to placebo ( $4.99 \pm 1.35$  nmol/l). ViNitrox could prevent the development of peroxynitrites, a harmful free radical (nitrotyrosin being a specific marker of peroxynitrites)."

And then there are the joints. "Arthritis is a type of inflammation that results in excess free radicals known as reactive oxidant species (ROS)," Quirk said. "Antioxidants can help reduce free radicals from inflammation and may help to improve joint health or comfort."

### Testing Methods

The list of benefits could go on, but, none of these benefits will get to consumers if the ingredients don't contain enough nutrients. A variety of tests exist to assay the amount of antioxidants in finished products; unfortunately, many disagree on which is the best method, and they all have their pitfalls. The oxygen radical absorbance capacity (ORAC) seems to be the most common measurement within the food industry; however, other antioxidant measurement tests are also used, including the Folin-Ciocalteu reagent, the Trolox equivalent antioxidant capacity assay, HORAC (hydroxyl radical), NORAC (nitroperoxyl radical) and SOAC (singlet oxygen quenching).

"It would be difficult to say which is most accurate because the level of antioxidant of a food is different based on which method is used," Chaudhari noted. "However, these test methods are good analytical tools and indicators to compare different ingredients in the marketplace. That being said, today, most labels that call out the product's antioxidant status reference an ORAC value."

Phillips said differing antioxidant capacity results will be obtained depending on what test method is used, but added ORAC is a good indication of in vitro antioxidant strength. "The ORAC method is still the gold standard, we believe. Our antioxidants are marketed and promoted with their ORAC values to promote a sense of standardization."

ORAC is fine for polyphenols, but not for fat-soluble products like vitamin E, according to Simmons. And, even when ORAC values are called out on labels, she said consumers won't understand its value. "ORAC alone is a good comparison, and it's good to have some comparison, but it wouldn't really mean much to a consumer if you made a label claim of an ORAC value of 1,200."

Lecareux said the scientific community is also questioning ORAC as a testing method. "It does not give any idea of the in vivo efficacy of the ingredients tested, she said. "In vivo or ex-vivo studies are necessary to confirmed antioxidant properties and bioavailability." As an example, she pointed out Bio Serae's ingredient Cacti-Nea™, a cactus fruit water extract with diuretic and antioxidant properties, has a low ORAC value. However, she said several studies confirmed the antioxidant properties of the ingredient. "This kind of scientific data can be considered as more important than an ORAC value; it is indeed much more relevant to assess the antioxidant benefit of an active in vivo than just in vitro."

Gitte Jensen, Ph.D., research director, NIS Labs, said these doubts in the ORAC test are causing marketers to use different types of information to promote antioxidant ingredients. “There is a growing awareness among natural products companies and regulatory agencies that ORAC doesn’t tell us how antioxidants work, and there is a push to get different types of data behind antioxidant products and to use more functional data in marketing efforts.” She added NIS Labs offers the Certified Bioavailable Antioxidants Program, which is a quality assurance program for antioxidant bioavailability.

Jensen said one of the mistakes product makers have made during the past few years was formulating to have the biggest ORAC value. “Now it is coming down to the understanding that if you really want to be a smart formulator, you’ve got to look broader,” she said. “You may have a good ORAC value, but your products may not do that much in people or in living cells.”

### **Formulation and Marketing**

Those claims, whether they be science-backed or not, are showing up on a wide variety of products, which means formulators are finding new ways to incorporate antioxidants into the lives of consumers. Jensen said she is seeing a big effort to expand beyond nutraceutical and capsules to food and beverages, like juices, milks, yogurt, candy and nutritional bars. “There is growing push in formulation to reach a broader market; for instance, those people that would pick up a food item, but would never pick up a bottle of capsules,” she said.

Simmons added ease is essential. “The consumer wants convenience and effectiveness. If a manufacturer can deliver something quicker or at a higher dose that can be absorbed quickly, the consumer will buy it.”

Whatever the end product, Rudi E. Moerck, president and CEO, Valensa, said antioxidant ingredients formulated for condition-specific applications, and antioxidants combined with krill, fish and plant oils are becoming more popular.

As far as where the antioxidants are sourced, it looks like botanicals are in the lead. Phillips said he is seeing exotic fruit and berry-derived ingredients from superfruits such as black currant, lingonberry, acai, noni and mangosteen. Lecareux added green tea and acerola to the list, but added she hasn’t seen scientific data on their positive results.

With many delivery forms and antioxidant sources, consumers may become inundated with options, which could pose problems for formulators. “Product differentiation is one of the key challenges in this market. The consumer is overwhelmed with choices. Making consumers aware of the science behind antioxidant performance is a difficult task with all of the products claiming antioxidant efficacy.”

Challenges for formulators go beyond consumer education, as incorporating these helpful ingredients can be difficult. First things first: the environment where these naturally derived ingredients may not cooperate. “Struggles and challenges often have to do with what Mother Nature has in store for crops,” Mosca said. “As antioxidants are derived from all manner of fruits and vegetables, harsh climate conditions will have impact at the front end.”

Then, once an ingredient gets into production, many issues can arise. “Many antioxidants are sensitive to light and heat, so when you’re processing, it’s important not to abuse them, and to try to provide the final product to the customer in the best possible shape from a stability and shelf life standpoint,” Simmons said.

While antioxidant-fortified beverages are popular, they offer their own formulation struggles. “A liquid product formulation can have problems and should have evidence of antioxidant stability within the liquid state because dissolved oxygen in water can cause a more rapid deterioration of antioxidant levels,” Quirk noted. “

Many companies use stability tests to ensure product label claims are accurate. For instance, Moerck said Valensa measures the amount of the antioxidant potential using Gas Chromatography (GC), Liquid Chromatography (LC) and UV, and additional spectrophotometric methods. Mosca noted PNI assays for both anthocyanins and proanthocyanadins via high performance liquid chromatography (HPLC).

Phillips noted as with any other category of supplements, marketers must be careful not to overstate claims, notably when it comes to condition-specific antioxidants. “It is important for manufacturers to keep claims simple and FDA compliant. Antioxidant science is a richly complex discipline on its own that can be quite befuddling to even the most inquiring of consumers. We recommend marketers work closely with technical writers who understand how to ‘translate’ the rich science to create and distribute more detailed literature for self-education purposes.”

Consumer education can only be a good thing for this market, as Jansen commented, “There’s opportunity for growth and I think that will stem from consumer education, and their knowledge of specific antioxidants for specific health conditions or staving off particular conditions. The term antioxidant is ubiquitous, but there is still a lot of confusion about which antioxidants are good for the eyes, skin or heart. It comes back to setting the consumer expectation and being upfront and truthful about what health benefits they can expect.”

As end-users learn more and establish appropriate expectations, the antioxidant-fortified product sales are expected to grow. Chaudhari said, “Because the term antioxidant resonates strongly with consumers, I believe that going forward, their inclusion in a product will be something that consumers will not only look for, but will serve as a point of determination as to whether or not that product is purchased.”

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