



PROGRESS IN THE CHOLESTEROL PUZZLE

While omegas and CoQ10 dominate store shelves for heart health, there are other strong contenders addressing cholesterol.

By Janet Poveromo

According to the American Heart Association, 34 percent of women and 52 percent of men have significant plaque buildup in their arteries (AHA, 2012). High cholesterol is inter-related with a number of other conditions (diabetes, obesity, high blood pressure) that contribute to overall cardiovascular health. "With heart disease being the leading cause of death in the U.S., we need to continue researching interventions that can prevent the development of these conditions," said Chief Scientific Officer Dr. Carl Hastings with Missouri-based Reliv International.

"Certainly dietary factors contribute to high cholesterol; however, many consumers are unaware that 80 percent of the cholesterol in the blood is naturally produced by the body in the liver," Hastings continued. "While some cholesterol is necessary for normal physiological and cognitive functioning, excess cholesterol is known to result in atherosclerosis, which contributes to CVD (cardiovascular disease)."

High rates of heart disease is not exclusive to the U.S. "There is a worldwide pandemic of chronic cardiovascular disease mediated, to a significant degree, by global increases in the prevalence of obesity, type 2 diabetes and the metabolic syndrome," noted Heather Thompson, marketing communications manager with Missouri-based Stratum Nutrition. "In Europe and the U.S., more than one in three adults currently live with one or more types of CVD, corresponding to 220 million and 81 million adults, respectively. Cardiovascular disease, especially atherosclerotic coronary heart disease and stroke, are the leading causes of death throughout the world."

Consideration must be given to various components that affect heart health. "Irrespective of one's genetic make-up, which certainly influences one's overall risk for developing CVD, appropriate lifestyle choices which include dietary modification, clearly result in a significant

risk reduction for contracting this dreaded disease," Thompson added. "Cholesterol in all forms (HDL, LDL, OxLDL and ratios of the above combined) are all measures by which we attempt to 'predict' the onset of CVD. As many people that have a cardiovascular event are within the 'normal' range of total cholesterol, research suggests that other factors must contribute (and should be evaluated) to the occurrence of such an outcome."

According to Dr. Alfredo Galvez, lead scientific advisor with Missouri-based Soy Labs, LLC, some of the "megatrends" that are driving the nutrition market in general are directly impacting this category. "An aging population, lack of confidence in traditional health care systems and globalization/consumer access to information are compelling shoppers to be proactive and seek alternative solutions to their health concerns," he said.

There are a number of factors keeping the market strong for products that address cholesterol. "The consumer awareness of 'cholesterol' being associat-



ed with CVD, combined with it being the leading cause of death, and consumers desire to maintain longer, healthier lives by ways of diet and supplementation keep the natural products market innovating products that address cholesterol and CVD," Thompson said.

Ingredient Market

The U.S. makes up the largest single heart health food and drinks market, capturing around two thirds of the overall sector (\$6.8 billion in 2009), and is forecasted to reach \$10.5 billion by 2015, said Pamela Stauffer, global marketing programs manager with Cargill Health & Nutrition in Minnesota.

"According to NMI, nearly three in four consumers report usage of heart-healthy foods and beverages. This trend has remained stable since 2005," she added.

And while omegas and CoQ10 may dominate "heart health" supplements, there are a number of additional nutrients that are expanding those options—phytosterols, resveratrol, lycopene, fibers

and soy proteins are a few focused on cardiovascular effects, Thompson pointed out. "Each tend to address various cardiovascular risk factors—whether cholesterol, OxLDL, triglycerides, blood pressure or even platelet aggregation."

Soy

"While the natural products market has seen a variety of bioactives that claim to reduce cholesterol, many of them lack the scientific evidence or a defined mechanism of action to substantiate their claims," Soy Labs' Galvez. "Soy protein, however, has an approved FDA health claim for cholesterol reduction. Recent evidence indicates that a naturally occurring soy peptide lunasin is the key component of soy protein that is responsible for the cholesterol-lowering effects observed in the meta-analysis studies cited that lead to the approval of the health claim." He added that a growing body of research shows that the lunasin peptide is one of the most important nutrition science break-

throughs related to cardiovascular health.

"Most cholesterol is produced in the liver by the HMG-CoA reductase gene. Statin drugs work by blocking HMG-CoA, but they can often block too much," Galvez explained. "This leads to serious side effects because our body needs a minimum level of cholesterol for proper cellular functions such as maintaining cell membrane integrity and hormone production." According to Galvez, lunasin works differently: it targets cholesterol at an earlier stage than statins, reducing the HMG-CoA without blocking it entirely. "Lunasin demonstrates superior support for cardiovascular health and exhibits significant anti-inflammatory properties," he added.

Reliv's LunaRich™ soy powder, launched along with Soy Labs this year, utilizes the lunasin peptide to balance cholesterol. LunaRich has been specially developed to contain five to 10 times the amount of bioactive lunasin as ordi-

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nary soy powders.

According to the company, 80 percent of cholesterol comes from the liver, so the most effective way to lower LDL (bad) cholesterol is to control the liver's internal production. The lunasin peptide does so in two ways:

- Selectively disrupts a step in the production of an enzyme key to cholesterol synthesis in the liver
- Increases the number of receptors available in liver cells to clear LDL cholesterol from the bloodstream

Compared to statins, lunasin works at an earlier stage in the process than prescription statins by reducing the expression of the HMG-CoA Reductase gene, according to Galvez. "Statin drugs work by blocking the HMG-CoA reductase enzyme after it has been produced when it's on its way to carry out the endogenous cholesterol production cycle. Statin drugs can oftentimes be too efficient and block too much of the HMG-CoA enzyme. As a result, serious side effects can occur."

Plant Sterols

Plant sterols and stanols are present



Products containing CoroWise

naturally in small quantities in many fruits, vegetables, nuts, seeds, cereals, legumes, vegetable oils and other plant sources. Studies have shown dietary plant stanols and sterols inhibit the absorption of cholesterol in the small intestine and decrease LDL-C. Plant stanols and sterols combined with statins further enhance the cholesterol-lowering effects.

"Plant sterols have been clinically shown to reduce LDL cholesterol and are backed by an FDA health claim," Cargill's Stauffer noted. "Consumers can look for the CoroWise® plant sterols logo on products to help identify those that can help lower their cholesterol."

Fiber

According to Thompson, Stratum Nutrition has done significant research on the effects of oxidized-LDL cholesterol on arteries. The company's ARTINIA® (chitin-glucan) is a fiber ingredient designed to support arterial health by

strengthening the body's natural antioxidant systems and defenses against OxLDL. ARTINIA has been the subject of multiple *in vitro* and *in vivo* human and animal studies, which collectively demonstrate the safety and tolerability of ARTINIA as well as its positive impact in decreasing OxLDL, she explained. "One of the most extensive, published animal studies involved a hamster model of nutritionally-induced atherosclerosis. This study demonstrated ARTINIA's positive impact on triglycerides, its enhancement of the activity of the important liver antioxidant enzymes, superoxide dismutase and glutathione peroxidase, and its influence in the reduction in cardiac production of superoxide anion (an important pro-oxidant compound)."

The most recent published human clinical trial has confirmed these safety data results that ARTINIA reduces oxidized LDL-cholesterol. The six-week intervention was a randomized, double-blind, placebo-controlled, multi-centered study utilizing an expanded range of human subjects in order to analyze oxidized LDL, lipids, glucose and insulin, along with other biomarkers of inflammation and human safety.

Ingredient Developments

The typical notion of product innovation, *(Continued on page 64)*

Ethical Naturals Completes Clinical Trial on Whole Grape Extract

In August, California-based Ethical Naturals Inc. (ENI), a supplier of botanical ingredients to the U.S. and international supplement, beverage and food markets, announced that, partnered with Canadian-based KGK Synergize, it has completed a randomized, double-blind, placebo-controlled clinical study that investigated the effect of ENI's patented whole grape extract on cholesterol and antioxidant status. The study included 26 human subjects exhibiting symptoms associated with one or more of the following conditions: pre-hypertension, and/or pre-diabetes.

Grapes and their corresponding extracts, with resveratrol, polyphenols, proanthocyanidins and flavonoids obesity have long been known to benefit overall health. The outcome of this study demonstrated that ENI's

whole grape extract has a positive effect on increasing HDL-C, and decreasing total cholesterol/HDL-C ratios in subjects after supplementation for six weeks. Key biomarkers reflecting oxidative stress, such as 8-isoprostane levels, were also improved in subjects using ENI's patented whole grape extract versus the placebo group. The extract was found to be safe and well tolerated at a dose of 350 mg/day in the population studied.

ENI has been granted a U.S. patent on this ingredient (U.S. Patent 7,959,963, June 2011) and the ingredient is patent-pending in China and the European Union. The whole grape extract is marketed under the brand names ORAC-15M™ and VinCare™, and it is standardized to contain 80 percent grape polyphenols with an ORAC Value of 15,000 μmol TE/gram.

VinCare and ORAC-15M are GRAS affirmed, and in addition to their use in supplements, are used widely for adding antioxidant value and polyphenol content to beverages. The extract is popular for this purpose because in addition to the high nutritional levels, the color and flavor profile are low, which is ideal for beverage use.

"We put a lot of work into developing this ingredient and obtaining the patent in the U.S.," said Cal Bewicke, president of ENI. "We're very pleased that this study scientifically validates the health benefits associated with products concentrated from whole grapes. In addition to being proven safe, healthy and effective, Ethical Naturals is confident that VinCare and ORAC-15M will continue to be excellent complements to its existing line of superior botanical ingredients."

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ance by implementing a number of quality control standard operation procedures, as well as becoming GMP certified. "GMP certification has had a positive impact on our industry; product development and marketing companies should insist on a manufacturer who is GMP certified," said Ravech. "In doing so, you can be assured that the facility has undergone third-party audits to ensure compliance with GMP standards and operating procedures."

"As long as antacids like Tums and H2 blockers like Pepcid are profitable, there is little incentive for major pharmaceutical corporations to market digestive enzymes. The same applies to the systemic enzymes," said Smith. "As

a result, enzymes will continue to grow as they have over the past two decades by word-of-mouth, recommendations from health practitioners open to alternative medicine and publications in the natural products industry. Finally, growth will continue because enzymes produce results you can actually feel." **NIE**

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FORMOREINFORMATION:

- American Laboratories, Inc., (402) 339-2494
- Deerland Enzymes, Inc., (800) 697-8179
- Specialty Enzymes and Biotechnologies, (909) 613-1660
- Triarco Industries, Inc., (973) 942-5100

Education

For Cargill's CoroWise brand of plant sterols, the company invests in a significant health care professional outreach program to arm key influencers with the information they need to educate patients about the cholesterol-lowering benefits of plant sterols, said Stauffer, adding that Cargill also goes direct to consumer in select marketing communications activities.

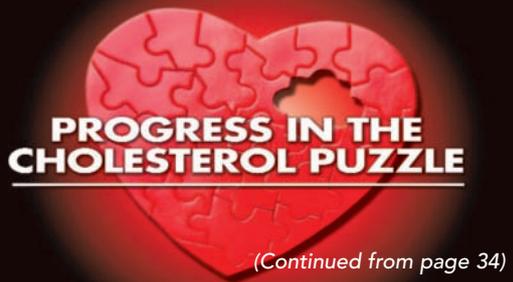
"It is critical that manufacturers help consumers develop a holistic and proactive attitude toward heart health," Hastings stressed. "Many of the conditions and risk factors that contribute to CVD are inter-related and are developed over time, so a targeted approach may not be the most effective. By encouraging consumers to strive for long-term overall wellness through sound nutrition, exercise and lifestyle choices, many of these conditions can be avoided." **NIE**

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Visit www.niemagazine.com to read about cholesterol and antioxidant levels' link to mortality.

FORMOREINFORMATION:

- Cargill, (952) 742-6080
- Ethical Naturals, (866) 459-4454
- Reliv International, (800) RELIV US
- Soy Labs, LLC, (573) 582-7388
- Stratum Nutrition, (888) 403-5039



"The heart health category is tricky because it is a category that no one can 'feel' the effects of," added Stratum's Thompson. "Innovations for new ingredients come out in the way of additional science support and education (of the industry, consumers and influencers) on how these ingredients affect one or more of the risk factors for CVD," she said. "The more we learn about the contributors and then effects of various ingredients on those is how innovative ingredients evolve."

"While cholesterol is an accepted biomarker for identifying the risk factors associated with cardiovascular disease, other potential biomarkers (e.g. inflammation markers, circulating free fatty acids, etc.) are being identified that may play an equally important role in heart health," Galvez agreed. "The key to future innovations in this segment will be finding bioactive compounds that work synergistically to support heart health by addressing the many inter-related health indicators."

Further, a new take on statins may be forthcoming. "Recently research is considering the use of low-dose statin treatment for primary prevention of cardiovascular disease," Galvez added. "In order to determine if statins are cost effective for patients at low CVD risk, researchers are weighing the adverse side effects of statins versus the benefits of reduced acute coronary incidents."

such as a unique delivery system, is not necessarily the primary focus of ingredients suppliers. "While new delivery systems are being developed, the target market for condition-specific, cholesterol-lowering products is still very accepting of the standard delivery formats," said Soy Labs' Galvez. "With the traditional formats of powders and capsules being the most cost-effective to manufacture, we have focused our research on validating the benefits of natural bioactives that have proven cholesterol-lowering properties."

The lunasin peptide found in LunaRich soy powder has been identified as the key component in soy that supports healthy cholesterol levels, Galvez said. New technologies have been developed by Soy Labs that enable the extraction and encapsulation of this soy peptide, he added. "This development represents a unique delivery format for soy preparations by concentrating the cardiovascular health benefits of 25 g of soy protein into a 250 mg capsule."