



Innovating
**FOR HEART
HEATH**

Reviewing ingredient science, regulations
and market considerations to drive
the heart health category



INGREDIENT MARKETPLACE

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Ingredients for Heart Health

The heart's dynamic needs require dynamic, effective solutions

by Rachel Adams

INSIDER's Take

- According to the American Heart Association (AHA), cardiovascular disease (CVD) is the leading cause of death globally.
- Natural ingredients improve blood lipid, cholesterol, glucose and more.
- Heart health as a target for sports nutrition applications may be an upcoming trend.

Cardiovascular disease (CVD) is a global problem. According to the American Heart Association (AHA), CVD is the leading cause of death globally, and accounts for 17.3 million deaths each year. What's more, AHA predicted that number will grow to more than 23.6 million by 2030.

Keeping the heart in top shape requires healthy blood lipid levels, cholesterol levels, blood pressure levels, blood glucose levels, flexible arteries and efficient circulation, to name a few considerations.

While lifestyle factors such as eating a healthy diet, exercising regularly and not smoking play a huge role in maintaining heart health, natural ingredients also have their place, and can help keep potential risk factors, such as blood pressure and cholesterol levels, healthy.

“One important fact to remember when we discuss heart health is, that there isn't just one important parameter we should watch for,” said Golan Raz, vice president of health and nutrition at Lycored (part of Adama Group). “Keeping our hearts in good shape requires a holistic approach and an understating that multiple factors are playing an important role.”

The benefits of **olive oil** on the heart are widely known, largely due to increased popularity and notoriety surrounding the Mediterranean diet—a diet favoring intake of olive oil versus butter and fatty fish versus poultry, along with high intake of fruits, vegetables, legumes and nuts. The Mediterranean diet alone has been associated with CVD prevention; when supplemented with olive oil, this diet has produced superior heart health benefits, such as improved high-density lipoprotein (HDL) cholesterol atheroprotective functions in humans¹ and reduced incidence of major cardiovascular events, as reported based on findings of the PREDIMED (Prevención con Dieta Mediterránea) trial.²

The PREDIMED trial was a parallel-group, multicenter, randomized trial including 7,447 Spanish participants who were at high cardiovascular risk, but with no CVD at



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enrollment, who were randomly assigned to one of three diets: a Mediterranean diet supplemented with extra-virgin olive oil, a Mediterranean diet supplemented with mixed nuts, or a control diet. Participants were followed for a median of 4.8 years.

Barbara A. Davis, Ph.D., R.D., vice president, medical and scientific affairs, PLT Health Solutions, referred to the 2013 PREDIMED study as “One of the most dramatic developments that has occurred in the area of heart health in recent years.” She added, “This study showed a relative risk reduction of approximately 30 percent among high-risk persons who were initially free of cardiovascular disease. As a result, interest in the Mediterranean diet—and some of its primary elements—exploded into consumer consciousness. This has been particularly true of olive oil.”

The heart healthy benefits of olive oil are attributed to the anti-inflammatory and antioxidant effects of its polyphenols, namely hydroxytyrosol, which offers strong radical-scavenging properties.³

“One of the most interesting compounds in olive oil for researchers is hydroxytyrosol,” Davis explained. “Along with tyrosol and their conjugates, [hydroxytyrosol] represents the main phenolic compounds in olive oil (50 percent). Hydroxytyrosol has a simple structure, the highest bioavailability and ORAC (oxygen radical absorbance capacity) of the olive oil components, which gives it potent natural antioxidant activity.”

Olive fruit polyphenol (as Hytolive®, from PLT Health Solutions) has shown anti-aggregating platelet action in humans,⁴ and inhibited in vitro platelet action in human whole blood.⁵ According to Davis, the recommended addition rate of Hytolive of 100 mg to foods, beverages and supplements contains hydroxytyrosol equivalent to 10 olives or 0.5 liter of extra virgin olive oil.

Spanish olive fruit extract (SOFE) improved blood vessel elasticity and reduced triglycerides compared to placebo according to a 2016 publication.⁶ In the double-blind, placebo-controlled study, 36 subjects were given either 50 mg/d of hydroxytyrosol (as Proliva® SOFE standardized to 20 percent hydroxytyrosol, from Euromed), 100 mg/d of hydroxytyrosol or a placebo. Arterial stiffness was measured using the Cardio-Ankle Vascular Index (CAVI). The higher 100 mg/d dosage provided the greatest protective effect of improving blood vessel elasticity and reducing triglycerides compared to individuals receiving placebo. Researchers concluded, “The decreased CAVI scores suggest that increasing high-density lipoprotein cholesterol and lowering triglycerides with SOFE could potentially reduce patients’ risk of developing atherosclerosis.”

In a double-blind, placebo-controlled study, Proliva was combined with a **red yeast rice** in a food supplement (as Cholesfytol®, marketed by Tilman SA) and administered to individuals with metabolic syndrome.⁷ Cholesfytol supplementation resulted in a 24 percent decrease of low-density lipoprotein (LDL) cholesterol, and a smaller but significant decrease of total cholesterol, ApoB and triglycerides. Oxidized LDL was reduced by 20 percent, and reductions in blood pressure were also found.



Guy Woodman, general manager of Euromed USA, pointed to an approval of a health claim in Europe as support for the body of research supporting the intake of olive oil polyphenols for heart health.

“The Panel on Dietetic Products, Nutrition and Allergies reviewed the research on polyphenols, including hydroxytyrosol contained in olive fruit and oil,” Woodman said. “The Panel concluded that ‘a cause-and-effect relationship has been established between the consumption of standardized olive oil polyphenols and protection of LDL particles from oxidative damage.’” To realize the benefits of this health claim, a minimum of 5 mg/d of hydroxytyrosol derived from olive oil should be consumed.

“The concentration of hydroxytyrosol in some olive oils due to adulteration with inferior oils may be too low to obtain this amount,” Woodman warned, and suggested supplementation as “a convenient and effective means to insure adequate daily intake of heart healthy olive polyphenols.”

Red yeast rice alone also benefits the heart. An extract of fermented products of patented functional red yeast strain *Monascus purpureus* NTU 568 (as AnkaScin® 568-R, from Sunway Biotech Co. Ltd.) reduced fasting blood glucose by 9.3 percent after 12 weeks of supplementation in a randomized, placebo-controlled clinical trial;⁸ helped regulate both systolic and diastolic blood pressure and lower triglycerides, increase HDL cholesterol and lower LDL cholesterol in hypertensive patients; and lowered serum cholesterol and LDL cholesterol by 11.1 percent and 20.4 percent after eight weeks of supplementation. The latter clinical trials are awaiting publication.

The cardioprotective benefits of long-chain omega-3 polyunsaturated fatty acids (LC-PUFAs) are well documented.



The product contains high levels of two active compounds—monascin and ankaflavin, said John Pan, president of SunWay Biotech Co. Ltd., which are the yellow pigments naturally produced by *Monascus* species.

The cardioprotective benefits of long-chain omega-3 polyunsaturated fatty acids (LC-PUFAs) including **eicosapentaenoic acid (EPA)** and **docosahexaenoic acid (DHA)** are well documented, with research spanning nearly 50 years.

“Early observations that LC-PUFAs promote cardioprotection were demonstrated in a series of prospective studies on Greenland Eskimos originating from the 1970s and 1980s,”⁹ said Kristine Sanschagrin, marketing manager, specialty seeds and oils, Cargill. “These studies revealed that the rarity of ischemic heart disease in this population was linked to their consumption of a diet high in LC-PUFAs from seafood.”

She pointed to a systematic review of the literature on the effects of LC-PUFAs on CVD outcomes, which found increased consumption was associated with reduced rates of all-cause mortality, cardiac and sudden death, and possibly stroke.¹⁰

Additionally, a recent meta-analysis of 18 randomized, controlled trials and 16 prospective cohort studies evaluated the effects of EPA and DHA on coronary heart disease (CHD), and found a statistically significant reduction in CHD risk in higher risk populations, including: 16 percent in those with high triglycerides and 14 percent in those with high LDL cholesterol; a non-statistically significant 6 percent risk reduction among all populations in RCTs, a finding supported by a statistically significant 18 percent reduced risk of CHD among prospective cohort studies.¹¹

Study authors suggested further clinical trials looking specifically at CHD outcomes may provide a better understanding of the promising beneficial relationship between EPA/DHA and CHD risk. The study was sponsored by the Global Organization for EPA and DHA Omega-3s (GOED).

Joseph Moritz, Ph.D., scientific marketing manager, BASF, suggested omega-3's role in inflammatory signaling contributes to many of its heart healthy effects. "Omega-3s are the precursors of anti-inflammatory signals that help to regulate inflammation wherever it occurs in the body," he said. "Through this and other mechanisms, they impact several biomarkers of heart health,¹² such as blood triglycerides,¹³ blood clotting¹⁴ and blood pressure."¹⁵ BASF's PronovaPure™ 46:38 EE delivers up to 90 percent omega-3 content and an EPA:DHA ratio of 46:38—a concentration that has been clinically studied in more than 100,000 patients, Moritz said.

The benefits of EPA and DHA are further supported by AHA's intake recommendations: 200 to 500 mg/d of EPA and DHA for adults, equivalent to a regular intake of two servings (8 oz. total) of fatty fish per week. Similarly, recommendations from the European Food Safety Authority (EFSA) suggest children over 2 years should consume 250 mg/d of EPA and DHA.

Multivitamins for Heart Health

"Although multivitamins are recommended primarily to fill nutrient gaps in the typical American diet, we saw particular interest in heart health in a prospective study last year that looked at a large cohort of [more than] 18,000 U.S. male physicians," said Joseph Moritz, Ph.D., scientific marketing manager, BASF Nutrition & Health. Results showed multivitamin users had a 6 percent decreased risk of major cardiovascular events with this reduction increasing to 44 percent in those that had taken multivitamins for more than 20 years at baseline. (*The Journal of Nutrition*. 2016;146(6):1235-1240.)



“However, of great concern is the fact that intake of natural sources of EPA and DHA, such as fish, averages well below that amount in the United States, at only 1.5 to 3 ounces per week, with lowest amounts consumed by teens,”¹⁶ Sanschagrin said, adding Cargill’s IngreVita™ EPA/DHA omega-3 oil can be added to foods and beverages to boost the nutritional benefits of the products.

Mark Stavro, senior director of marketing, Bunge, cited the Dietary Guidelines for Americans to further support the benefits of polyunsaturated fats. “According to the 8th and most recent version of the Dietary Guidelines for Americans, strong and consistent evidence from human studies shows that replacing saturated fats with unsaturated fats, especially polyunsaturated fats, can reduce LDL cholesterol and the risk of coronary heart disease,” he said. “Canola oil is a great choice for getting unsaturated fats, including polyunsaturated omegas-3 and -6 fatty acids.”

Chia ingredients are a rich source of alpha-linoleic (ALA) fatty acids, which are largely responsible for some of the heart healthy effects of chia. Sandra Gillot, CEO, Benexia, pointed to research supporting chia’s ALA content in lowering blood pressure, improving coagulation factors and decreasing inflammatory markers,¹⁷ as well as lowering triglycerides levels and increasing HDL cholesterol.^{18,19} Further, ALA in chia seeds induced lipid redistribution associated with cardioprotection and hepatoprotection.²⁰ Chia seeds traffic lipids away from the heart and liver and increase their accumulation in visceral fat.

According to Gillot, Benexia’s chia yields the highest amount of ALA fatty acids.

A product derived from the sap of the *Angelica keiskei* plant (as ChalCurb™, from Japan Bio Science Laboratory) reduced visceral fat at a dose of 200 mg/d (in an unpublished, randomized, double-blind, placebo-controlled study); improved circulation in rats by inhibiting phenylephrine-induced vasoconstriction via endothelium-derived relaxing factor (EDRF) and/or nitric oxide (NO) production;²¹ and ameliorated the elevation of blood glucose levels in mice that develop hyperglycemia upon aging,²² among other benefits.

According to Vincent Hackel, MBA, president and CEO, Japan Bio Science Laboratory, the product’s effects are attributed to its naturally occurring, bioactive flavonoids called chalcones. The company currently has two 60-subject, blind, placebo-controlled studies in process on the ingredient, he said.

Healthy Tubes

Certain carotenoids including **alpha-** and **beta-carotene** can benefit the heart. Dietary intakes of alpha-carotene and beta-carotene were inversely associated with CVD mortality, according to a 15-year CVD mortality study involving 939 elderly men (Zutphen Elderly Study, funded by the Netherlands Prevention Foundation).²³ Additionally, the third National Health and Nutrition Examination Survey Follow-up Study (NHANES III) reported serum alpha-carotene concentrations were inversely associated with risk of death from all causes, including CVD.²⁴



Chia seeds traffic lipids away from the heart and liver and **increase** their accumulation in visceral fat.

GRAPE SEED EXTRACT FOR CARDIOVASCULAR HEALTH BENEFITS



MegaNatural[®] BP

grape seed extract —
blood pressure maintenance

- Three clinical studies support the effectiveness of MegaNatural[®]BP in improving blood pressure
- Efficacy shown for delivery via supplements and beverages
- Patented
- All natural
- Water soluble
- Highly pH stable
- GRAS approved
- Non-GMO
- High ORAC values

MegaNatural[®]BP is a patented FDA no-objection GRAS grape seed extract shown to help support blood pressure levels that are already within normal range, and helps support normal arterial function. **MegaNatural-BP supports healthy blood pressure levels in subjects with pre-hypertension.**

The product is made in California from a special seed blend derived entirely from unfermented domestic red and white varietal wine grape seeds. The seeds are extracted with hot water, purified, concentrated and spray-dried with no carrier, resulting in a high phenolic, high ORAC grape seed extract powder without any preservatives. MegaNatural[®]BP is ideal for use in supplements and in functional foods and beverages.

Human studies conducted at the University of California, Davis, Department of Preventive Cardiology showed that a 150-300 mg per day dose reduces systolic and diastolic rates after six weeks. This original research provides support for blood pressure structure/function statements.

For more information on MegaNatural[®]BP, contact your PLT Health Solutions representative, or visit us at www.PLTHealth.com; keyword – MegaNatural-BP.



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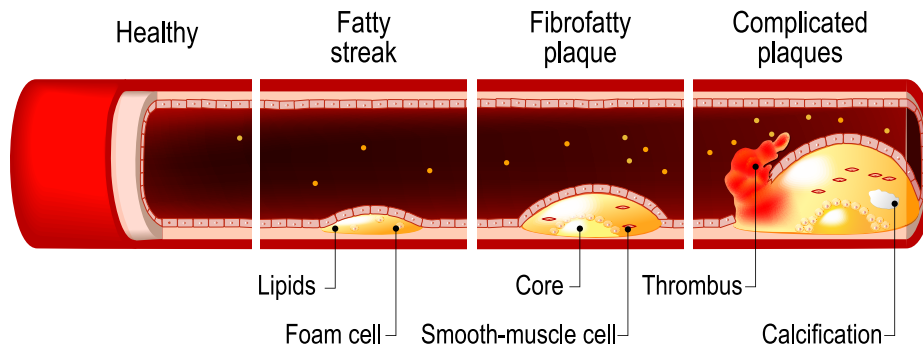
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HEALTH SOLUTIONS

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A 2013 publication indicated an association between serum levels of carotenoids (specifically **lycopene**, alpha-carotene and beta-carotene) and atherosclerotic progression in 840 men aged 46 to 65 years from Eastern Finland.²⁵ After seven years of follow-up, researchers reported the three carotenoids studied showed inverse association with maximum intima-media thickness—a biomarker of atherosclerosis, or hardening of the arteries.

Atherosclerosis increases the risks of heart attack, stroke and death related to CVD. Atherosclerosis occurs when plaque builds up within the arteries and then hardens, limiting the flow of oxygen-rich blood to the heart and body and also increasing the risk of clot formation within the arteries, which can lead to heart attack. Plaque is made up of fat, cholesterol, calcium and/or other substances in the blood.

Stages of Atherosclerosis



Bryan See, regional product manager, ExcelVite Inc., pointed to new research indicating plasma carotenoids such as alpha-carotene, beta-carotene and lycopene were significantly reduced with age.²⁶ "However, for females and non-smokers with high consumption of vitamin supplements, fruits and vegetables, they demonstrated significantly higher level of alpha-carotene in the plasma—indicating that nutritional supplementation of alpha-carotene, as well as dietary carotenoids intake, are crucial for maintaining adequate alpha-carotene level in the body," he said, and noted ExcelVite's EVTene™ offers a high concentration of alpha-carotene (approximately 35 percent) and provides a solution for manufacturers looking to develop a mixed-carotene product to address heart health.

In a randomized, controlled human clinical trial, bioenhanced palm tocotrienol complex (as EVNol SupraBio™, from ExcelVite Inc.) improved arterial compliance in healthy adults.²⁷ For the trial, 36 healthy volunteers were randomized to receive either a placebo or a palm tocotrienol complex at doses of 50 mg, 100 mg or 200 mg daily for two months. Measurements for arterial compliance (carotid femoral Pulse Wave Velocity and Augmentation Index) and other parameters, such as blood pressure and serum lipid profile, were taken before and after treatment. Results showed a statistically significant improvement in Augmentation Index (up to 8.7 percent reduction from baseline) was observed in all tocotrienol-supplemented groups. A significant improvement in Pulse Wave Velocity (up to 10 percent reduction from baseline) was also seen in subjects who received 100 mg and 200 mg of palm tocotrienol complex.

Vitamin K2 (as MenaQ7® Vitamin K2 as MK-7, from NattoPharma) decreased arterial stiffness in post-menopausal women administered 180 mcg/d for three years, compared to placebo, which experienced a slight increase.²⁸

“Results confirmed that MenaQ7 not only inhibited age-related stiffening of the artery walls, but also made a statistically significant improvement in vascular elasticity,” said Eric Anderson, senior vice president global sales and marketing, NattoPharma USA Inc. According to Anderson, this study showed vitamin K2 (as MenaQ7) can “switch on” undercarboxylated (inactive) matrix Gla protein (MGP) already present in the body. “Once activated, MGP inhibit calcium from depositing in blood vessels and arteries, which can contribute to cardiovascular problems,” he explained. “By activating these proteins, vitamin K2 contributes to improved cardiovascular health via endothelial function.”

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**Heart Health
Marketplace**

Want to learn more about vitamin K's impact on cardiovascular disease (CVD)? Attend the “The Relationship Between Vitamin K and Cardiovascular Disease” session as part of the Education Programme at Vitafoods Europe, May 9-11, in Geneva, for an in-depth look at the research behind vitamin K's heart healthy effects.

For consumers who are inclined to develop arterial calcification, Anderson said vitamin K2's protective effects were more significant. A study published in 2014 evaluated whether higher doses of MK-7 (MenaQ7) supplemented for a longer duration would result in a more pronounced activation of MGP in individuals with vascular calcification and showing high levels of undercarboxylated MGP. In this study, 200 individuals took 360, 720 or 1,080 mcg of MenaQ7 three times weekly for eight weeks.²⁹ Researchers found MK-7 supplementation dose-dependently reduced undercarboxylated MGP. The levels decreased by 17 percent, 33 percent and 46 percent, respectively.

Healthy Cholesterol Levels

There are two types of cholesterol, HDL, or “good” cholesterol, and LDL, or “bad” cholesterol. LDL cholesterol contributes to plaque build-up, which can lead to atherosclerosis. HDL cholesterol, on the other hand, helps remove LDL cholesterol from the arteries.

“It is known that as the size of cholesterol particles decreases, the cardiovascular risks increase,” said Steve Holtby, president and CEO, Soft Gel Technologies Inc. “One of the most important metabolic markers is a small, dense form of LDL. Their small size makes it easier to enter the arterial walls, where they can cause damage and create other cardiovascular issues.”

Cholesterol isn't inherently bad, but must be maintained at appropriate levels to keep blood flowing properly to the heart. High levels of LDL cholesterol can lead to clogged arteries, which can be more easily blocked by potential a blood clot, and could result in heart attack or stroke.

See pointed to research supporting **tocotrienol**, which degrades a key enzyme that regulates the cholesterol synthesis pathway—HMG-CoA reductase—leading to reduced cholesterol levels in the liver.³⁰

A study comparing EVNol SupraBio and alpha-tocopherol supplementation at 50mg/d for four weeks found tocotrienol supplementation produced a statistically significant decline in total and LDL cholesterol levels compared with the alpha-tocopherol group. Although there were no significant changes in HDL cholesterol and triglyceride levels in both groups, a net decline in triglyceride level was observed in the tocotrienol group compared with a net increase in the alpha-tocopherol group.³¹

In a double-blind, placebo-controlled human study published in 2011, 32 hypercholesterolemic subjects were administered either 300 mg EVNol SupraBio or placebo capsules containing 300 mg soy bean oil for six months.³² Results showed tocotrienol supplementation reduced total cholesterol by 8.9 percent while LDL cholesterol decreased 12.8 percent after four months of supplementation, compared to baseline. After six months of supplementation, total cholesterol and LDL cholesterol reduced by 10.8 percent and 17.3 percent, respectively. By contrast, subjects in the placebo group had negligible changes in total and LDL cholesterol levels compared with baseline.



Tocopherol-free tocotrienol derived from the annatto plant (as DetlaGold®, from American River Nutrition) combined with AHA Step-1 diet significantly reduced total cholesterol by 15 percent, LDL cholesterol by 18 percent, triglycerides by 14 percent and cytokines associated with CVD between 39 and 64 percent at an optimal dose of 250 mg/d.³³

Additional research published in 2002 showed daily supplementation with 200 mg tocotrienols from three commercially available sources for 28 days did not result in a significant change in blood lipid concentration in men and women with hypercholesterolemia.³⁴

Pantethine is a derivative of pantothenic acid (**vitamin B5**). A review and analysis of published studies from 1966 to 2002 on subjects with abnormally elevated lipid levels who were given an average of 900 mg/d of pantethine (as Pantestin, from Kyowa Hakko) showed an 8 percent increase in HDL cholesterol, a 20 percent decrease in LDL cholesterol and a 33 percent reduction in triglycerides after four months.³⁵

According to Elyse Lovett, marketing manager, Kyowa Hakko U.S.A. Inc., pantethine initiates antioxidant activity and is more metabolically efficient than pantothenic acid. “It also provides a safeguard against excessive blood lipid production,” she said. “Pantethine helps increase the metabolic activity of coenzyme A and the acyl-carrier protein (ACP) which creates a reduction in cholesterol synthesis.”

A bergamot (**Citrus bergamia Risso**) polyphenolic fraction (BPF, as Bergamonte®, from HP Ingredients)—containing bioactive compounds standardized to more than

38 percent polyphenolic flavanoids consisting of naringin, neohesperidin, neoeriocitrin, 1 percent melitidin and 2 percent brutieridin—was evaluated in a study involving 237 individuals who either had isolated hypercholesterolemia, mixed hyperlipidemia (elevated lipids levels in the blood, including cholesterol), or metabolic syndrome.³⁶ In the 30-day, placebo-controlled study, participants were given either placebo, 500 mg of BPF or 1,000 mg of BPF. The supplement led to a strong reduction in total cholesterol, LDL, and a significant increase in HDL in the majority of the subjects. No significant changes in the mean cholesterol parameters were recorded after 30 days in the placebo groups.

According to a 2013 publication, a 1,000-mg dose of Bergamonte significantly enhanced the hypolipidemic effect of the statin drug rosuvastatin compared with the effect of rosuvastatin alone; triglycerides were reduced by 42 percent and HDL was increased by 34 percent, an effect which was significantly higher compared to use of rosuvastatin alone.³⁷ The study also supported Bergamonte's vasoprotective action via its antioxidant ability.

Bergamonte decreased the mean concentration of intermediate density lipoprotein (IDL) particles by 51 percent, to increase large LDL by 38 percent, and to decrease small LDL by 35 percent, according to a 2014 publication.³⁸

A carotenoid-rich **tomato extract** (CRTE, as Nutrient Complex for Heart™, from LycoRed) increased carotenoids levels in plasma and improved oxidized LDL response to a high-fat meal in healthy, normal weight individuals in a randomized, double-blind, parallel-groups, placebo-controlled study published in 2016.³⁹ For the study, 146 individuals were randomly assigned to a daily dose of CRTE standardized for tomato phytonutrients or placebo during a period of two weeks. Oxidized LDL, glucose, insulin and triglyceride responses were measured for eight hours after ingestion of a high-fat meal before and at the end of intervention. Plasma lycopene, phytofluene and phytoene increased throughout the study period in the CRTE group compared to placebo. CRTE ingestion significantly improved changes in oxidized LDL response to high-fat meal compared to placebo after two weeks, but there were no significant changes observed in glucose, insulin or triglyceride responses.

Plant sterols—compounds found in fruits, vegetables, seeds and nuts—“reduce bad cholesterol [LDL] in the body by blocking the absorption of cholesterol into the bloodstream,” said Pam Stauffer, global marketing programs manager, Cargill.

Health Canada reviewed 84 randomized, controlled trials (published from 1994 to 2007) in its Summary of Assessment of a health claim supporting plant sterols' ability to lower cholesterol, and concluded: “Overall, an 8.8 percent reduction in LDL cholesterol was observed with an average intake of 2 g/d of plant sterols. A dose-response relationship was observed up to about 3 g/d in these studies which included doses ranging from about 0.5 g/d to 9.0 g/d. At the average intake of 2 g/d, the effect of plant sterols appeared to be largely independent of the food matrix.”



Health Canada approved the claim for plant sterols: “[Serving size] of [product] provides X% of the daily amount of plant sterols shown to help reduce/lower cholesterol in adults,” with 2 g of plant sterols representing the daily amount.

Additionally, FDA published a Proposed Rule in 2010 to amend the regulation authorizing a health claim on the relationship between plant sterol esters and plant stanol esters and reduced risk of coronary heart disease (CHD). The amendment would expand the types of foods that can bear the claim to include a broader range of foods, modify the daily dietary intake of the substance specified in the claim as necessary for the claimed benefit, and adjust the minimum amount of the substance required for a food to bear the claim, among other changes.

“You know the science is sound when the FDA recognizes the beneficial role of plant sterols by authorizing a health claim associating them with the reduced risk of heart disease,” Moritz commented. BASF’s Vegapure™ plant sterols have demonstrated cholesterol reduction in a variety of formats such as margarine, dietary supplement and beverages, he said.

Health Canada approved the claim for plant sterols.



Stauffer said Cargill’s CoroWise® plant sterols are a concentrated form of this plant compound “that can be used by food, beverage and supplement manufacturers to formulate products for consumers looking to help maintain a healthy heart.” Its plant sterols do not affect the taste or texture of food and beverages.

Holtby pointed to research showing high dietary intake of **citrus juice** (orange or grapefruit) has been shown to reduce hypercholesterolemia—an effect attributed to the flavanone glycosides hesperetin from oranges and naringenin from grapefruit.⁴⁰

“In addition to these flavanones, citrus also contain PMF; the most common ones are tangeretin and nobiletin,” he said. PMF lowered cholesterol and triglycerides in hamsters with diet-induced hypercholesterolemia.⁴¹

A patented formulation of PMF and tocotrienols (as Sytrinol®, from Soft Gel Technologies Inc.) lowered total cholesterol by 20 percent, LDL cholesterol by 22 percent, and triglycerides by 28 percent.⁴² “PMF modulate lipoprotein and lipid metabolism directly in the liver, by decreasing apoprotein B needed for endogenous synthesis of LDL-cholesterol, and inducing the suppression of diacylglycerol acyltransferase, an enzyme required for triglycerides synthesis.” Holtby said.



Fiber from **whole grains** has been associated with improved cholesterol. A meta-analysis of 24 randomized, studies published in 2015 concluded consumption of whole grain diets lowers LDL and total cholesterol.⁴³

“Shifting from refined grains to whole grains can increase dietary fiber, and a number of human studies collectively provide evidence that eating soluble dietary fiber can help lower LDL cholesterol,” Stavro said.

Statins and CoQ10

Statin drugs are commonly prescribed to help lower cholesterol levels in hypercholesterolemic patients. However, statin drugs have been shown to deplete **coenzyme Q10 (CoQ10)** levels in the body, indicating the need for supplementation.

“Both cholesterol and CoQ10 share a common biosynthetic pathway, which involves the formation of mevalonate compound with the aid of 3-hydroxy-methylglutaryl coenzyme A [HMG-CoA] reductase,” Steve Holtby, president and CEO, Soft Gel Technologies Inc., explained. “Inhibition of HMG-CoA reductase by statin drugs at the mevalonate level will inevitably decrease the levels of both cholesterol and CoQ10.”

Human studies revealed a significant decrease in CoQ10 serum levels as a result of HMG-CoA reductase inhibitor treatment. In a double-blind, randomized clinical trial, hypercholesterolemic patients received either Lovastatin or Pravastatin (statin drugs) over a period of 18 weeks (*Mol Aspects Med.* 1997;18:S137). At the end of the study period, the total serum level of CoQ10 declined by about 25 percent in the Lovastatin and Pravastatin groups.

CoQ10—found in virtually all cells of human body including the heart, liver and skeletal muscles—functions as a carrier to transfer electrons across the membrane of mitochondria (the energy generator in the body’s cell) to drive the production of adenosine triphosphate (ATP), the fuel that energizes cells in the body. “Heart muscle cells have the greatest concentration of mitochondria, 5,000 per cell,” Holtby said. CoQ10 is an antioxidant, he added, and may improve oxygen uptake in the mitochondria of the heart.

Soft Gel Technologies’ CoQsol®—a softgel formulation of CoQ10 that includes antioxidant ingredients such as beta-carotene and mixed tocopherols—has been demonstrated in clinical research to improve serum levels of CoQ10 and a preclinical trial demonstrated it was preferentially absorbed into heart cell mitochondria, the energy source for the heart. It’s CoQsol-CF® is a crystal-free softgel formulation of CoQ10 offering a rate of absorption 550 times higher compared to CoQ10 powder, according to an unpublished, human clinical trial. Its CoQH-CF® is designed to protect ubiquinol—the reduced form of CoQ10—from being oxidized and allows individuals who are unable to process CoQ10 effectively on their own to increase plasma levels of CoQ10 in its reduced form.



Healthy Blood Pressure

Blood pressure, the force exerted by blood on the arterial walls, is measured at two points: systolic blood pressure is measured when the heart contracts, and diastolic blood pressure is measured when the heart is at rest.

High blood pressure, or hypertension, can cause several problems in the body, including damage to the arteries via microscopic tears caused by the excessive force of blood, more rapid hardening of the arteries and increased build-up of materials such as cholesterol, platelets, fats and plaque. Eventually, damaged, hardened arteries can lead to damaged organs, blood clots and CVD.

Grapeseed extract (as MegaNatural®-BP, from Polyphenolics/PLT Health Solutions) reduced systolic and diastolic blood pressure rates in patients with metabolic syndrome at a dose of 150 or 300 mg/d after six weeks of supplementation,⁴⁴ and lowered systolic and diastolic blood pressure rates in pre-hypertensive patients at a dose of 300 mg/d for eight weeks.⁴⁵

In a randomized, double-blind, two-arm, parallel, placebo-controlled trial published in 2016, a beverage containing MegaNatural-BP improved blood pressure in pre-hypertensive patients.⁴⁶ Thirty-six subjects were randomized to placebo or grapeseed extract groups, and consumed a juice containing placebo or 300 mg/d of grapeseed extract (150 mg twice daily) for six weeks. Grapeseed extract significantly reduced systolic blood pressure by 5.6 percent and diastolic blood pressure by 4.7 percent, which was significantly different (systolic) or tended to be different (diastolic) from placebo. Subjects with higher initial blood pressure experienced greater blood pressure reduction—nearly double the effect size.

Grapeseed extract reduced systolic and diastolic blood pressure rates in patients with metabolic syndrome.

“MegaNatural-BP modulates heart health by upregulating endothelium nitric oxide synthase (eNOS), and by doing so, increases nitric oxide levels in the cardiovascular system,” Kennedy said. “The physiological response to this is an increase in endothelium elasticity which helps support healthy vasodilation and blood flow thereby helping to maintain healthy blood pressure levels.”

Nattokinase (as NSK-SD®, from Japan Bio Science Laboratory) reduced inflammation as measured by C-reactive protein (CRP) in adults at risk for CVD;⁴⁷ reduced diastolic and systolic blood pressure levels in hypertensive men and women in an eight-week, randomized, controlled trial;⁴⁸ improved circulation compared to baseline in healthy men and women 80, 120 and 180 minutes after consumption;⁴⁹ and enhanced fibrinolysis and anti-coagulation via several different pathways simultaneously in healthy males.⁵⁰





Heart Health in Sports Nutrition

Targeting a healthy heart for sports nutrition applications may be on the horizon in the category.

Golan Raz, vice president of health and nutrition at Lycored (part of Adama Group), said the company is in the process of finalizing the results from its recent efforts in the field of cardio and sport nutrition. “This program is both important and exciting mainly because of the growing number of people who are actively increasing the amount of weekly workouts they do,” he said. “While there are many benefits to this trend, there are also some side effects and these side effects are getting the attention of the creative R&D teams in Lycored.”

Additionally, new research showed **Indian tree (*Terminalia arjuna*)** bark extract significantly increased cardiovascular efficiency and improved cardiac conditioning in young, healthy male adults, according to a double-blind, placebo-controlled, randomized clinical trial published in the *American Journal of Therapeutics* (online ahead of print, November 2016). For the trial, 32 healthy male subjects were administered either 400 mg Indian tree bark extract (as Oxyjun™ developed by Enovate Biolife Pvt. Ltd.) or placebo for 56 days. The effect of the product was evaluated by ECG and graded exercise protocol. After exercise protocol, researchers assessed the left ventricular ejection fraction, right ventricular myocardial performance index, and Borg Rated Perceived Exertion (RPE) at baseline, day 28 and day 56. Cardiac biomarkers creatine kinase and troponin-T were assessed to determine cardiomyocyte insult. On day 56, the Oxyjun group reported the exercise conducted was easier and less stressful than the placebo group. The Oxyjun group exhibited significant improvement in cardiac conditioning as evident by ECG, which was responsible for improvement in the measured exercise performance. Oxyjun is supplied by IN Ingredients and distributed in North America by Prinova.



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