



# Maestro for Cardiometabolic Harmony

# BERGAMONTE

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When Metabolic Syndrome throws the body out of balance, it's like the music of the spheres being in chaos. A maestro is needed to bring back functional harmony.

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## BEING HEART HEALTHY

pantethine, pomegranate extract, aged garlic extract, fibers, RYRE (red yeast rice extract) and plant sterols.”

Bergamot is especially influential, due to both its vitamin C and polyphenol component.

“Bergamot, the Italian citrus fruit (largely abundant in the Calabria region), has a set of compounds that research shows can get to the heart of the MetS [metabolic syndrome] matter—it has shown ability to positively influence specific factors,” said Annie Eng, CEO, Florida-based HP Ingredients. “Bergamonte BPE Complex, a standardized extract of Citrus *Bergamia* *Risso*, is rich in polyphenols, such as neoeriodictine, naringine, neohesperidine, melitidine [and] brutieridine. It also contains a high amount of both pectin and vitamin C.”

Eng also noted that Bergmonte BPE Complex’s mechanisms of action (MOA) include:

- Inhibiting the enzyme HMG-CoA reductase
- Inhibiting enzymes known as phosphodiesterases
- Activates adenosine monophosphate-activated protein kinase (AMPK)
- Activates cholesterol 7 $\alpha$ -hydroxylase
- Inhibits expression of pro-inflammatory cytokines
- Regulates hunger/appetite hormonal expression (leptin, ghrelin and adiponectin). This MOA was just discovered in 2019.

According to Prinova USA (Illinois), the company often deals with ingredients such as vitamin C, magnesium, potassium, mixed tocopherols (vitamin E), niacin, CitraPeak (hesperidin), astaxanthin, vitamin K2, CoQ10, along with standardized beet juice powder, some of which’s demand is on the rise.

“In general, the demand for antioxidants continues to grow; examples include CoQ10, astaxanthin, vitamins C and E,” pointed out Jayesh Chaudhari, MS, MBA, senior director of research and development. “These antioxidants chelate the free radicals from the body, which results in reduced chances of heart disease. CoQ10 is a potent antioxidant, which helps protect LDL [low-density lipoprotein] from oxidation. This subsequently contributes to reduction in atherosclerosis. Studies have shown that CoQ10 at 200 mg per day with a high load of omega-3 fatty acids (EPA [eicosapentaenoic acid] and DHA) significantly reduced blood pressure, markers of inflammation, and lipid levels. Another

antioxidant, astaxanthin from microalgae, is the most powerful antioxidant, known to reduce oxidative stress and improve blood lipid profile and capillary circulation. It is 6,000 times stronger than vitamin C, 3000 times stronger than resveratrol, 800 times stronger than CoQ10, and 500 times stronger than vitamin E. Potassium (K), magnesium (Mg) and calcium (Ca) are some of the key minerals, which help control high blood pressure. K is important for muscle function, including relaxing the walls of blood vessels. This lowers blood pressure and protects against muscle cramping. Mg helps regulate hundreds of body systems, including blood pressure control. Ca is important for healthy blood pressure because it helps blood vessels tighten and relax, as needed.”

He continued, “Niacin (vitamin B3) may



help to raise good high-density lipoprotein (HDL) cholesterol and remove bad low-density lipoprotein (LDL). Recent studies showed that water-dispersible CitraPeak (citrus flavonoids) at 200 mg per day exerts the vasodilation effect by producing NO [nitric oxide]. In the coming years, there will be more demand for the use of probiotics as a preventative dietary approach for cardiovascular.”

### Ingredient Innovation & Safety

A major task by manufacturers is verifying that ingredients are used to the best of their abilities during formulation.

“While natural astaxanthin has extremely potent antioxidant properties, it is sensitive to degradation,” explained Tryggvi Stefánsson, COO, Algalif (Iceland), manufacturers of astaxanthin ingredients. “Studies have shown that astaxanthin formulated with lipid

carriers is more stable.<sup>1</sup> Algalif, for example, uses a clean process to add sunflower oil as a lipid carrier liquid which helps preserve its antioxidant capacity. Another study suggests that a lipid environment helps to enhance of the antioxidant capacity of astaxanthin.”<sup>2</sup>

DSM (New Jersey) has tackled innovation by designing omega-3 that not only suits multiple lifestyles, but is making its presence known in a plethora of products internationally.

“What began as a NASA research project years ago has led to the development of a vegetarian, sustainable source of DHA omega-3. Our life’sDHA is a vegetarian, kosher, halal and major allergen-free DHA sourced from algae that is non-genetically modified and is the only DHA currently used in U.S. infant formulas,” said Hugh C. Welsh, president and general counsel, DSM North America. DSM’s life’sDHA has been the subject of more than 100 research studies during the past two decades, has supported the nutritional needs of more than 60 million babies and is now found in over 500 food, beverage and supplement products around the world.”

ExcelVite’s ingredients come from non-GMO Malaysian sustainable palm oil—its EVNol SupraBio and EVNolMax products offer several delivery methods to choose from, allowing consumers to decide which method better suits his or her needs.

“Technology advancement has allowed for ingredients to take different forms for the ease of formulation and delivery dosage form,” noted Bryan See, the New Jersey and Malaysia-based company’s business development manager. “As an example, heart health benefits of EVNol SupraBio patented and bioenhanced palm tocotrienol complex may be delivered via softgels (direct encapsulation); or formulated into a vitality drink product through a powder tocotrienol form—EVNolMax. For older individuals who are unable to swallow pills, taking a ready-to-drink product will allow them to receive the benefits in a convenient way for them.”

Louisiana-based Alfasigma offers an L-carnitine solution under its MitoCarn brand, which is substantiated by various safety claims.

“MitoCarn Heart is a 100 percent active, high concentration L-carnitine solution with defined mechanisms of action,” said Vaughn DuBow, MitoCarn brand manager, whose product is available in a capsule, gel, gummy, liquid, powder and tablet. “These are supported by clinical studies using healthy populations. One of the key differentiators with MitoCarn Health is its quality standards. MitoCarn offers the most stringent quality, transparency and supply chain controls





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possible. Every aspect revolving around the production of MitoCarn is clearly documented and made available to customers, which includes batch specific certificates of analysis (COA) confirming test methods and declarations showing the absence of toxins, pesticides, allergens, GMO, irradiation and nanomaterials. MitoCarn also provides Kosher and Halal certification to ensure that others can benefit from our ingredients around the globe. MitoCarn has been able to maintain, if not exceed, exceptional quality and research standards to really stand out from the market at large."

New Jersey-based OmniActive Health Technologies, manufacturers of CurcuWin, a natural turmeric curcuminoid extract, uses flow mediated dilation (FMD), "a process that reflects the ability of blood vessels to relax during increased blood flow," to quantify curcumin's effect.

"We believe applying FMD as a way to measure curcumin's impact on heart health is novel," Brian Appell, marketing manager, said. "And it is particularly relevant for supplement products that are geared to supporting healthy consumers. Given that CurcuWIN has been studied in healthy individuals makes the benefits and claims directly transferable to supplement products.

"It should also be noted that generic curcumin can also bring its share of formulation challenges," he added. "In other words, because it has poor solubility and absorption, large doses of standard curcumin powder are typically needed for health benefits. In a placebo-controlled, crossover study comparing commercial curcumin products, CurcuWIN increased relative absorption of total curcuminoids 46 times over standard curcumin. Produced using OmniActive's proprietary UltraSOL Nutrient Delivery System, CurcuWIN contains the same profile as found naturally in turmeric. This translates to smaller doses and better delivery."

### An Encompassing Market

The heart health market continues to develop as consumers are taking more of a proactive—rather than reactive—approach.

"The heart healthy supplement consumer demographic has evolved, and there is a significant emphasis on preventative measures in addition to addressing pre-existing health concerns," observed Kate Pastor, SVP Superba Sales America, Aker BioMarine

Antarctic US LLC (New Jersey). "It's not only about trying to manage or reduce risks in those with pre-existing heart conditions, it's about lifestyle changes and taking the simple steps to being a healthier version of yourself while you are still healthy. Omega-3s are often sought after as part of a heart health solution, but I think that they are actually becoming more of a baseline nutrient supplement similar to a multi-vitamin type nutrient or probiotic intended for overall health and wellbeing.

"As product innovation evolves and companies like Aker BioMarine continue to invest in clinical research, I am confident that we will see growth in this category," she continued. "As we have seen in the mainstream nutraceutical market, as well as in

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— Kate Pastor, Aker BioMarine  
Antarctic US LLC

pharmaceuticals, omega-3s have a positive impact and it's not unique to fish oil. Krill oil has been a clinically researched omega-3 option for heart health and more for a few key reasons. Krill is rich in omega-3 fatty acids: essential for heart health as well as a wide range of health benefits for your eyes, liver, skin, brain and more. And unlike other omega-3 options, krill is naturally bound to phospholipids, preserves itself with astaxanthin in its organically occurring composition and is an ideal source of choline."

Statistics are successful in demonstrating the impact that heart-related conditions can have, and they ought to be taken seriously.

"The increasing cases of mortality rate due to cardiovascular diseases are raising the demand for heart health products globally," explained Rachela Mohr, manager business development for nutraceuticals at Germany-based WACKER, Wacker Che-

mie AG. "According to the World Health Organization (WHO), 17.9 million people die from cardiovascular disease (CVD) each year, which accounts for 31 percent of all deaths worldwide. This makes CVD the world's No. 1 killer. According to Market Research Future, the global heart health products market is estimated to grow by more than 6.5 percent by 2022. The U.S. is a key market holding a major share. According to the American Heart Association, an American will have a heart attack approximately every 40 seconds. About 35 percent of American adults are living with some form of cardiovascular disease or the after-effects of stroke. Due to this situation, there is a great need for products that have a positive effect on heart health. The most typical ingredients for creating heart-healthy food, for example, are plant stanols and sterols. In cereals, such as oats and barley, beta-glucans are known for their ability to lower blood cholesterol and insulin resistance. Ingredients, including fibers and garlic extract, are chosen for their benefits as it regards to cardiovascular health. A recent study also indicates the beneficial effects of hydroxytyrosol, a polyphenol especially known from olives."<sup>3</sup>

It is apparent the consumers are continuously in search of ingredients and products that are supported by scientifically validated research, so it is important for manufacturers to be constantly conscientious of that.

"The market for heart-healthy ingredients is strong and we only see it growing going forward," predicted Christopher Speed, senior vice president of global sales and marketing with NattoPharma (New Jersey and Norway). "Heart health is one of the core categories where consumers begin to consider supplementation, so providing formulations that feature nutrients clinically validated to support heart health is an important consideration for manufacturers."

### Research

Aker BioMarine is utilizing its success with krill oil to immerse itself into other markets, with the hopes of impacting more consumers.

"Superba Krill is one of the most researched krill oil brands on the market, with several studies documenting its efficiency in raising the Omega-3 Index in the body, and we are currently working on some new and exciting research projects and partnerships," Pastor said. "In fact, Aker BioMarine is supplying krill oil as a core ingredient to be used by biopharmaceutical innovator Acasti Pharma Inc. to create its CaPre development prescription drug, a highly purified omega-3 phospholipid concentrate, designed to treat severe hypertriglyceridemia. A chronic,



metabolic condition that contributes to the increased risk of cardiovascular disease and pancreatitis, hypertriglyceridemia affects an estimated one third of the U.S. population alone.

"The fact that pharmaceutical companies are looking at krill oil as a therapeutic option for the management of cardiometabolic disorders proves that the potential is there, and that companies like Aker BioMarine have the opportunity to take this heart health market to new levels and reach the folks that can benefit from it the most."

Heart health entails a plethora of data and research, so the challenge lies in focusing on the proper topics that suit one's interests.

"Research into cardiovascular function is a very complex field," noted Shastri. "Many researchers have spent decades studying atherosclerosis, but without understanding of arteriosclerosis. My research has centered on understanding the pathophysiology of atherosclerosis, which occurs when arteries harden and fill with plaque. There are many classical risk factors for atherosclerosis, but the main actors can be distilled into a simple phrase: oxidized and elevated cholesterol. Elevated cholesterol levels provide the foundation for lipid migration into the arteries, and also increases the size of fatty deposits in your blood vessels. Not all cholesterol ought to be targeted—HDL cholesterol, for instance, is responsible for removing circulating cholesterol and transporting it to the liver.

He noted, "Kaneka has been deeply involved in cardiovascular health for decades, since we are one of the most recognized providers of ubiquinone and ubiquinol (Coenzyme Q10) in the world. A few years ago, our company began a deep dive into the world of probiotics with the launch of a probiotic portfolio formulations called Floradapt."

Natreon, who as referenced earlier offers Sensoril and Capros for cardiovascular health, has conducted research with both ingredients, which has brought back a variety of results.

Natreon's patented Sensoril Ashwagandha is shown to promote heart health by improving the augmentation index 91 percent compared to placebo, as well as support cardiac function and support healthy blood pressure and blood lipids already within the normal range,<sup>4,5</sup> Brown pointed out. "These improvements in heart health are contributed to the bioactives found in the leaves and roots of ashwagandha, unique to Sensoril," Brown said.

Clinically studied Capros, an aqueous extract of *Phyllanthus emblica*, also called amla, is another patented Natreon ingredi-

ent that has been clinically shown to improve blood vessel function and support healthy blood flow.<sup>6</sup> In addition to the studies in healthy subjects, Capros has also been studied in type 2 diabetics showing even more significant heart healthy results. Along with improvements in blood vessel function and blood flow, Capros has been shown to significantly increase nitric oxide—a key marker in improved blood vessel function and blood flow.<sup>7</sup>

Stefánsson noted that the studies demonstrating astaxanthin's impact is readily available.

"Studies continue to consistently indicate positive results for astaxanthin's ability to reduce oxidative damage and inflammation as well as to provide additional heart health benefits such as improved blood flow," he said.

While Pastor noted the impact that krill is making, fish oils in general remain prominent for heart health.

"Omega-3 EPA and DHA are among the most popular heart healthy ingredients, and every day, the research on EFAs grows as scientific researchers examine new potential benefits associated with fish oil consumption," said Welsh. "While the science is still emerging in some areas, the research supporting the benefits of omega-3 EPA and DHA for heart, brain, eye and maternal health is strong, and there is a high level of consumer awareness of the importance of nutritional lipids. Since omega-3 cannot be produced by [the] human body, it has become increasingly important for manufacturers to source ingredients in a sustainable manner in order to meet the rising demand. As one example, we support a renewable, sustainable environment by sourcing fish for MEG-3 oils from regulated fisheries where equipment, practices and procedures are in place to protect fish stocks. The fish oil we use is sourced from a variety of wild fish species and is a by-product of either the fishmeal or edible canning industries. No fish are caught for the exclusive production of oil. We also turn fish oil processing waste into biofuel to operate our state-of-the-art fish oil production facility in Mulgrave, Nova Scotia."

Synthetic ingredients were once almost a standard in products targeting cardiovascular health, but over the years, there has been a shift to natural; consumers are not only seeking items backed by science—they demand ones that are beneficial for the environment too.

"Many years ago," concluded See, "synthetic ingredients used to be popular in heart health products, such as beta-carotene and dl-alpha-tocopherol as described in

the famed CARET® and HOPE/HOPE-TOO® clinical trials respectively. However, these synthetic ingredients proved harmful to subjects in the studies, and subsequently, manufacturers and consumers turned their focus to natural ingredients. Thanks to the Millennial-driven clean label movement coupled with increased consumer awareness and demand for evidence-based products, manufacturers now source ingredients that are produced in a sustainable manner, with scientifically substantiated health benefits in order to meet these trends and demands." **NIE**

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