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Reviving the omega-3 market
Omega-3 remains a leading category within the nutraceutical

industry, however, minimal innovation and evolving consumer behaviour has created a stagnant market. Companies experiencing declining sales are having to think big to reform the market, drive innovation and create new opportunities for the future omega-3 category.

How vitamin K2 puts calcium in balance

Exercise, lifestyle and the avoidance of known risk factors all affect cardiovascular health. Securing the right balance of heart-healthy nutrients, including vitamin K2, is another proven way to reduce cardiovascular risk. **Jim Beakey** explains how K2 works to balance calcium, ultimately promoting improved cardiovascular health.

Black garlic extract for heart health

Fluctuating diet patterns and varying

Fluctuating diet patterns and varying levels of active lifestyle among the 30- to 40-year-old age group is expected to generate more awareness of heart health. Additionally, a rise in the geriatric population has created various opportunities for the cardiovascular market. **Alberto Espinel** highlights a new ingredient for the heart health market that specifically targets atherosclerosis.

Takeaways



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Taken to heart

The heart is an incredible organ—beating over 100,000 times a day to pump roughly five litres of blood throughout our body. We often overlook how important it is to take care of our heart, and most of us don't kick up a fuss until we have to.

According to the World Health Organization, ischaemic heart disease and stroke have remained the world's greatest causes of death over the last 15 years—by a long shot. As a result, health practitioners and associations have been proactive in educating the public about how taking steps to support heart health improves quality of life and reduces the risk of myriad chronic conditions. It's never too early to start looking after your heart and thankfully, there's a multitude of preventative and management solutions.

While a healthy diet and exercise are key to improving heart health, more consumers are looking to dietary supplements and functional foods to deliver cardiovascular benefits.

Omega-3 solutions are the go-to solution when we initially look to put long-term preventative measures in place. Essential fatty acids are key to improving and maintaining heart health, and with an increasing link to cognitive health and prevention of other conditions—like lupus, eczema and arthritis—omega-3 supplements are increasingly considered for their range of benefits. Despite this, crowded shelves, undifferentiated offerings and poorly-backed health claims have caused the omega-3 market to stagnate. Consumers are also confused about how to select a supplement best suited to their needs. Every person's omega-3 needs are different and the amount of long-chain eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) needed to raise omega-3 index will vary from person to person—enter personalised nutrition. We explore challenges and opportunities for omega-3 market growth on page 4.

Alongside other essential minerals like magnesium, copper and zinc, calcium balance has an important role in the body—but too much of a good thing can actually adversely affect cardiac health. In the spotlight time and again for its calcium plaque reduction powers is vitamin K2. Jim Beakey identifies K2 as the heart's answer to calcium regulation, and provides an overview of the relationship between K2 and arterial calcification on page 8.

Finally, an emerging ingredient for heart health is aged black garlic extract. Ingredient and market expert Alberto Espinel walks us through how the extract's antioxidant effects interact in the body to deliver cardiovascular benefits—supported by multiple clinical trials.

There's a long way to go to reverse the global leading cause of death statistic, but with growing public awareness and innovative solutions at the surface, we may just move the needle a little bit each year.



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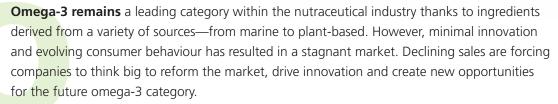
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Reviving Omega-3s

Exploring challenges and opportunities for market growth

By Charlotte Bastiaanse



Sources

The three types of omega-3 fatty acids known to deliver health benefits to humans are alpha-linolenic acid (ALA), commonly found in plant oils, and eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which can be produced by the body from ALA and are found preformed in fish oils and marine plants. Animal-derived sources of EPA and DHA include fish, fish oils, eggs from chickens fed EPA and DHA, squid oils, krill oil, and certain algae. With an increase in consumers choosing plant-based diets for health and animal welfare concerns, marine algae and phytoplankton have become popular primary sources of omega-3 fatty acids. ALA is typically found in the plant oils of various nuts, seeds, legumes and grains, including walnuts, flaxseed, linseed, soybean, and hemp.

What makes omega-3 fats special?

The human body can make most of the types of fats it needs from other fats or raw materials, but this isn't the case for certain fatty acids. These essential fats cannot be manufactured by the body on its own, making ingestion in the diet critical. Educated consumers know the benefits of eating foods high in omega-3: fatty fish like salmon and tuna, vegetable oils, various nuts and seeds, and leafy vegetables.

Omega-3s are an essential part of cell membranes throughout the body and affect the function of the cell receptors in these membranes.¹ They provide the starting point for making

hormones that regulate blood clotting, contraction and relaxation of artery walls, and inflammation.¹ They also bind to receptors in cells that regulate genetic

function. Decades of research also support that omega-3s help to prevent heart disease and stroke, lowers blood pressure, can help control health conditions such as lupus, eczema, and rheumatoid arthritis, and may

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play protective roles in cancer and other conditions.1 Most recently, omega-3s are being increasingly investigated and promoted for their sleep, memory and general cognitive health benefits.1

Finished product challenges

Omega-3 levels can be increased through diet, but the easiest way to ensure consistent and sufficient intake is through daily dietary supplementation. Although health conscious consumers and those with certain health conditions understand the benefits of upping their omega-3 intake, a recent study by Euromonitor examined countries including the U.S., United Kingdom (UK) and China, and found most individuals were not getting enough of the daily recommended amount of omega-3 fatty acids.²



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Experts have highlighted various consumer-centric reasons for a weakening omega-3 market:

Overcrowded shelf

One need only browse the shelves of local pharmacies or wellness stores to see the significant competition amongst omega-3 products. Consumers are easily overwhelmed by too much choice, with no clear differentiation between products.

EPA and DHA content

Major health organisations recommend 250-500mg of EPA and DHA intake per day for healthy adults,³ but this may be increased for individuals targeting health conditions especially cardiovascular concerns. There is an abundance of products on the market that do not meet minimum requirements. Smart consumers quickly lose trust in labels displaying insufficient content or promoting generic health claims.

Undifferentiated products

Tied back to overcrowded shelves, consumers are not spoilt for choice when it comes to how they get their omega-3 intake. Formulation challenges mean omega-3s are conventionally offered in capsule and softgel format. New formats like gummies have more momentum in the market but are challenged with delivering high DHA and EPA content.



The opportunity for delivery format innovation

Pill fatigue is an industry-wide challenge as consumers move away from pills and actively seek their supplements in the form of a food or beverage. Protein and probiotic ingredient experts, for example, have a far easier opportunity to differentiate finished product offerings yet still meet requirements for effective delivery. Gummies, lozenges, health shots, functional beverages, snack bars and cereals are amongst the favourite forms.

Beyond the search for alternative delivery format, conventional omega-3 capsules and softgels are challenged by three key hurdles:

- 1. Too big and difficult to consume
- 2. Unpleasant taste
- 3. Unpleasant smell

Developers know there is an opportunity in the market to deliver alternatives, but new formats come with challenges of their own:

- · Insufficient levels of active ingredient
- Finished product stability
- Doubt over efficacy
- Lack of supporting research

A rise in consumers concerned about sustainably and ethically sourced omega-3 oils (especially from marine life) as well as a radical shift toward vegan and vegetarian diets mean that plant-based omega-3 products are expected to boost the overall market in coming years. While softgels, capsules and oils derived from fish oils remain effective and reliable formats for optimal intake, the good news is that plant-based sources also offer new powder application opportunities for future product differentiation.



End consumers typically do not know to take an omega-3 supplement together with their fattiest meal of the day to activate enzymes and increase absorption.

Educating consumers

Beyond overcrowded shelves causing confusion, an added challenge for the market is connecting with consumers to promote the value of omega-3 supplements and remind them of the health benefits delivered through long-term supplementation. Supplement users often look for results they can measure in the short-term, so when consumers don't notice an immediate difference in the way they feel, there is increased risk they fall into irregular patterns or stop intake altogether.

Additionally, consumer understanding about how and when to take omega-3 supplements is of paramount importance. As well as the finished product label, consumers need to have resources available that educate them on how fats are digested by the body.

Although commonly known to product developers, end consumers typically do not know to take an omega-3 supplement together with the fattiest meal of the day in order to activate enzymes and increase optimal absorption. The challenge here is consumers tend to avoid fatty meals and younger consumers are notorious meal-skippers.

Essentially, an omega-3 supplement is a shot of pure fat. When consumed on an empty stomach, the body does not recognise the supplement as a meal and, as a consequence, the fat emulsifies in the stomach causing digestive discomfort. An unpleasant experience may cause a consumer to change or stop their supplement habits, so readily available and abundant information about how and when to supplement is of paramount importance for omega-3 brands.

Changing supplement habits

Across the various micro markets within the nutraceutical industry, consumer behaviour is changing and brands are challenged more than ever before with closing the gap between the supply chain and the end consumer. Brands are seeking new marketing channels and investigating alternative methods to connect to consumers.

Stagnant markets have an opportunity to revive themselves not only through ingredient and product innovation, but also through how closely they understand consumers, educate them, and provide solutions that meet universal and individual needs.

Because long-term health and prevention benefits of omega-3s are undeniable, experts predict that efforts geared toward improving consumer education, reducing shelf confusion, and providing validated products will drive future growth for the category.

During the BASF UK Customer Innovation Day held on 18 September, 2019, omega-3 innovation expert Ove Wikstrom promoted the message of driving growth through market penetration. In order to deliver more omega-3 to more consumers, Wikstrom highlighted three consumer types and how to combine innovation with marketing to overcome current challenges.

Non-consumers:

Innovation: Make it easy to start and maintain a new habit Marketing: Educate on benefits and best practices for intake

Lapsed consumers:

Innovation: Provide next-level product performance **Marketing:** Remind and reconvince consumers of benefits

Current consumers:

Innovation: Provide superior product performance

Marketing: Reward loyalty with insight

Finally, proof of health claims in the form of clinical research or data is essential for securing supply chain and end customer trust and loyalty. With pharmaceutical businesses entering the space, standards are being raised across the industry and only businesses willing to invest in research that backs label claims will win the competition for shelf space. It may be an expensive investment to convince and convert consumers, but even more so to win them back once they're lost.

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Cardiovascular health is certainly influenced by genetics, but behaviour and environment also play important roles. Exercise, lifestyle and the avoidance of known risk factors all affect cardiovascular health. Securing the right balance of heart-healthy nutrients, including vitamin K2, is another proven way to reduce cardiovascular risk.

Vitamin K2 and calcium

The essential mineral calcium is vital to bone-building, muscle function and other biological processes. But for all its benefits, calcium is also at the root of two of the leading causes of cardiovascular disease (CVD). Too much calcium in the body can lead to hardening of the arteries and vessels of the cardiovascular system, making them less flexible. Calcium plaque can also build within arteries and vessels. These types of tissue calcification make the heart work harder and increases the risk of cardiovascular incident. Fortunately, there is an essential vitamin which helps keeps calcium in balance.

Daily supplementation of vitamin K2, ideally as menaquinone-7 (MK-7), is a positive behaviour that can improve cardiovascular health. Vitamin K2 regulates calcium in the body. It does this by activating matrix Gla proteins (MGP), which bind excess calcium in the bloodstream and prevent calcium from being deposited in cardiovascular tissues. K2 also regulates calcium by ensuring that it is used for bone-building by activating the proteins responsible for integrating calcium into the bone matrix.

Calcium and CDV risk

When calcium begins to build-up in the circulatory system, arteries and vessels begin to stiffen. This reduced elasticity and flexibility, in the worst cases, results in a condition called arteriosclerosis. As calcification progresses, the heart must work harder to push blood through vessels that may also be partly blocked calcium plaques (atherosclerosis). Hardened vessels also lose their ability to expand outward and the risk of rupture increases. This type of calcification is a predictor of cardiovascular disease, and is progressive, usually developing over decades. It is also common, as some degree of calcification may exist in as many as one-third of people over the age of 45.2 Stiffening generally increases with age, and increases CVD risk regardless of age.3 Calcium is vital for bone health, but the body needs to regulate how calcium is utilised to prevent unhealthy consequences for the heart.

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How Vitamin K2 MK-7 puts calcium in balance

Vitamin K2 is the heart's answer to calcium regulation. K2 activates osteocalcin proteins which transport calcium into the bone matrix, supporting calcium's bone-health role. However, to balance against the effects of excess calcium, vitamin K2 also activates the calcium-binding protein MGP.⁴ Activated MGP binds excess calcium in the blood and prevents it from being deposited in arteries.⁵

Top K2 heart studies

The relationship between vitamin K2 and arterial calcification is strong. High levels of non-activated MGP are correlated with lower vitamin K intake and lower survival rates among cardiovascular patients.⁶ Daily K2 supplementation at 90 µg doses has also been shown to decrease levels of non-activated MGP⁷⁻⁹ and increase activated MGP levels.¹⁰

The strongest evidence for the preventive role of K2 in cardiovascular health comes from the Rotterdam study. Nearly 5,000 Dutch men and women, age 55 and higher, took part in the study for between 8 and 11 years. Diets high in vitamin K2 were shown to dramatically reduce CVD risk and mortality.¹¹ Another study followed 16,000 women aged 40 to 79. This study demonstrated an inverse correlation between dietary K2 and heart disease, and specifically a 9% reduction in CVD mortality risk for each additional 10 µg/day of K2 intake.¹²

A 2015 study by Knapen *et al.* concludes that beyond prevention, vitamin K2 can reverse existing levels of calcification and restore arterial flexibility. Knapen showed that high intake of vitamin K2 MK-7 was linked to reduced arterial calcification.¹³ Further, it demonstrated that arterial stiffness significantly decreased in the MK-7 test group after three years (180 μ g/day), compared to a slight increase for the control group.



A 2015 study by Knapen et al. concludes that beyond prevention, vitamin K2 can reverse existing levels of calcification and restore arterial flexibility

K2 from diet or supplementation?

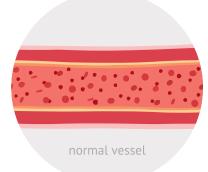
Western diets are likely K2 deficient,¹⁴ creating opportunity in a wide range of market categories. Vitamin K2 (menaquinone) is actually a family of molecules with side chains of different lengths. EFSA approval, however, is limited to the MK-7 form. Studies demonstrate that MK-7 is best for supplementation because it is absorbed best and is most bioactive.^{8,14,15-17}

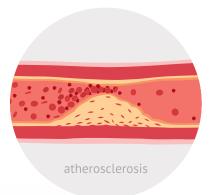
The MK-7 molecule exists in nature, but in some respects is uncommon. Most dietary K2 consists of less efficient MK forms in meat and dairy products, but in levels too low to meet requirements. This dietary deficiency may be a relatively recent development brought about by changes in food preservation and livestock management. Regardless, vitamin K2 is an essential fat-soluble vitamin that is vital at all stages of life. Supplementation is an effective solution, and MK-7 is the best, most bioactive K2 form.

Vitamin K2 heart health formulations

Vitamin K2 balances calcium, but the body requires several other important nutrients for cardiovascular health. Multi-ingredient heart health products can leverage the synergistic benefits of several nutrients to reduce the risk of cardiovascular disease. Magnesium, for example, is an essential mineral that regulates cardiac function, rhythm and vascular muscle tone. B-complex vitamins also contribute to normal heart function. The K2VITAL® Bone₄Kardio™ white-label product is an example of a multi-ingredient formulation that leverages K2, D3, magnesium and B vitamins for both bone and heart health.

L-arginine is an amino acid that relaxes blood vessels and lowers blood pressure. Omega-3 fatty acids are also important. The body needs both omega-3 and omega-6 fatty acids for optimal heart health. Western diets are high in omega-6 (from vegetable and soybeans oils) and low in omega-3 (from fish). Formulations like OMEKA-3, designed by Kappa Bioscience and CAPSUGEL, provide K2 and omega-3 in an innovative dosage form. The vitamin K2 market is growing rapidly, and vitamin K2 offers commercial opportunity in multiple market categories.





Jim Beakey has been promoting the bone and heart health benefits of Kappa Bioscience's K2VI-TAL® vitamin K2 MK-7 for several years. Before that, Jim had a long career in research-based business consulting—primarily for the healthcare and pharmaceutical industries. K2VITAL® vitamin K2 MK-7 is a pure all-trans K2 that is identical to the MK-7 found in nature. It works with the body to put calcium in balance. Microencapsulated K2VITAL® DELTA allows K2 to be formulated with calcium or magnesium in heart health and multivitamin products which can meet K2 potency claims for full shelf-life.





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Emerging ingredient for heart health

New-generation aged black garlic extract for every beat of your heart

by Alberto Espinel



Heart health global market insight

Within dietary supplements, it's thought that those specifically developed for cardiovascular health are amongst the most consumed and sought after by consumers—growing in relevance year by year. Fluctuating diet patterns and varying levels of active lifestyle among the 30- to 40-year-old age group is expected to generate more awareness of heart health, as well as shed light on current solutions and offerings for consumers to consider. Additionally, a rise in the geriatric population (estimated 962 million people globally aged over 60-years-old, with the majority being in Europe) has created various opportunities for the cardiovascular market.

New market opportunities

The heart health market is focused on addressing and preventing well-known risk factors associated with cardiovascular disease. However, there are still unexplored opportunities when it comes to the control or improvement of new markers related to the development of cardiovascular diseases. Additionally, there are emerging opportunities of new products targeting consumers where pharmacological drugs do not produce the desired effect or align with consumer health preferences.

Risks associated with heart failure

The heart beats approximately 50 to 100 times per minute, and at an average of 2.5 billion times throughout life as the heart continuously works to push litres of blood to all parts of the body. This constant flow transports oxygen, hormones, and other compounds to all the cells that form the body, additionally eliminating waste metabolism products. Because of this, if the heart stops, failure of virtually all body functions is likely to occur. Among the different factors that can cause heart failure, poor diet, lack of exercise and smoking remain areas of concern associated with modern day lifestyle.

A condition known to increase risk of heart failure is atherosclerosis: the accumulation of plaque (made up of fat, cholesterol, calcium and other substances) in the wall of the arteries. This accumulation produces a decrease in the diameter of the arteries, limiting the passage of blood that is pumped by the heart. Greater problems occur when this cholesterol plate breaks apart and travels through the blood vessels until it clogs smaller arteries, such as those that supply the heart and the coronary arteries – limiting its blood supply and causing potential onset of a heart attack or stroke.

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Emerging ingredient for heart health

Garlic to the rescue

While garlic has been discussed for years for its heart health benefits, the mechanism of action and specific beneficial compounds have been less known. One targeted compound is the antioxidant S-allyl cysteine, which has been studied for its cardiovascular benefits in multiple clinical trials.^{2,3} The antioxidant properties are produced by the garlic itself through a single chemical reaction, or 'autocatalysis'.4 On the other hand, included in the different polyphenols present in the finished ingredient, melanoidins are macromolecules responsible for the dark colour of aged black garlic, which exert antioxidant effects that are beneficial to the lipid profile.5

A new aged black extract ingredient (ABG10+, from Pharmactive Biotech Products) is standardised to ≥0.1% S-allyl cysteine through high performance liquid chromatography (HPLC). This optimised ageing process is responsible for its unique composition in bioactives (S-allyl cysteine and polyphenols). The ingredient is backed by science as a highly stable and bioavailable biomolecule that works to reduce oxidative damage through its potent antioxidant and cardioprotective properties.^{5,6} The extract helps to maintain proper functioning of the heart, as it is able to increase the heart's contraction force by inducing dilatation of the coronary arteries, allowing a greater flow of nutrients to the heart that to maintain optimal activity.6

Under conditions of obesity-induced hypercholesterolemia, a one-month treatment of ABG10+ resulted in a 22% decrease in LDL (low-density lipoprotein) cholesterol circulating levels, reducing the risk of atheroma plague formation. Additionally, the level of the beneficial HDL (high-density lipoprotein) cholesterol increased by 46%, thus improving the HDL/LDL ratio by 70%. These promising results suggest that supplementation with this unique compound could help maintain proper heart function, helping its normal daily activity and decreasing the risk of atherosclerosis.

Currently, the aged black garlic extract ingredient has been successfully adapted for formulation of finished products, and suitable as a supplement or in functional foods. Such an ingredient has the potential to meet the consumer demand for natural alternatives that target the comprehensive care of main cardio-metabolic alterations.

Alberto Espinel is Head of R&D at Pharmactive Biotech Products S.L.

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Takeaways for your business

Heart health is a far-stretching concern, affecting millions of people across the globe. Thankfully, there's an abundance of solutions—with a significant rise in plant-based.

The vast population of people adopting vegan and vegetarian diets—or those purely reducing their meat intake—naturally lower their risk of early heart disease onset, but that's not to say that's where solutions end. Plant-based ingredients also present new product and delivery format opportunities. Omega-3 supplements are conventionally derived from marine animal sources and offered in capsule, softgel or oil drops format, but the increasing range of plantderived sources formulated for powder applications could create points of differentiation in the market. Although we may see a range of functional foods and beverages in the future that overcome taste hurdles, the question of efficacy and sufficient fatty acid content will undoubtedly challenge future developers.

Plant-based ingredients may offer differentiation in omega-3 products, but it can't be ignored that the greater market is facing flatline challenges. With consumer behaviour changing on an almost constant basis, developers and brands have to work tirelessly to attract, educate and maintain omega-3 supplement users. Crowded shelves and a multitude of finished products lacking proven claims has caused consumer confusion and competition amongst brands. Omega-3 businesses will grow through market penetration and through their ability to address the individual needs of non, lapsed and current consumers.

Beyond healthy fats, consumers are also curious about the benefits offered through essential vitamins and minerals. Calcium, magnesium, zinc, copper and zinc are amongst the necessary minerals for the body, targeting different health areas. Although necessary for healthy bones and muscle function, too much calcium can harden the arteries and vessels of the cardiovascular system, making them less flexible. Calcium plaque can also build within arteries and vessels. Calcification makes the heart work harder and increases the risk of cardiovascular incidents. Vitamin K2 has proven benefits of keeping calcium in balance and regulating its content in the body, and if developed in combination with other ingredients—like D3, magnesium and B vitamins—can be even more impactful in targeting heart and bone health.

Beyond vitamins and minerals, there's an abundance of natural foods that deliver benefits to our heart. Fatty fish, nuts, seeds, grains, berries, beans, berries and tomatoes are some of the well-known foods that everyone should consider in their everyday diet. Garlic is another food with science on its side and a known ability to reduce blood pressure and cholesterol levels. While garlic has been discussed for years for its heart health benefits, the mechanism of action and specific beneficial compounds have been less known. One targeted compound is the antioxidant S-allyl cysteine, which has been studied for its cardiovascular benefits in multiple clinical trials. A new aged black garlic extract has been identified as a highly stable and bioavailable. Clinical studies have proven that the extract works to reduce oxidative damage through its potent antioxidant and cardioprotective properties. Such an ingredient has the potential to meet the consumer demand for natural alternatives that target the comprehensive care of main cardio-metabolic alterations.

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