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# Heart Health: AT THE HEART OF THE MARKET

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Heart health has consistently ranked as one of consumers' top five health concerns. **Irene Wolfhart**, senior consultant at analyze & realize, examines the existing products and innovation potential in the European heart health market.

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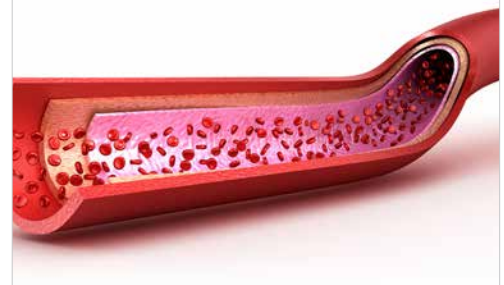
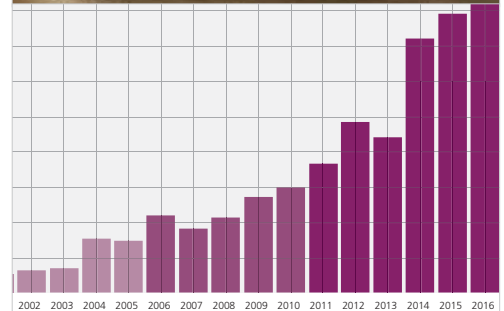
Although nutritional supplementation has been shown to effectively reduce the risk of certain chronic conditions, studies rarely consider the healthcare cost savings of such interventions.

**Patrick Coppens**, director regulatory and scientific affairs at Food Supplements Europe, details the results of a study highlighting the potential healthcare cost savings from the daily use of phytosterols in people with severe hypercholesterolemia.

### 17 Vitamin K2: Vital for Life and Wellness

As **Jim Beakey**, marketing director at Kappa Bioscience, explains, there's more to a cardiovascular health than just the prevention of severe cardiovascular disease—vitamin K2 is a vital component in ensuring a healthy circulatory system and optimal heart health.

## 22 Takeaways



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# Have Your Heart Set on Health

**F**or something so vital, most of us take heart health for granted. Perhaps it's the ever present ba-dum, ba-dum we feel, lulling us into a false sense of security that everything's okay; perhaps we take the 'it won't happen to me' approach to heart health.

Unfortunately, heart disease is the leading cause of death among women in the United Kingdom, kills 3.9 million Europeans every year, and accounts for 45 percent of all deaths in Europe. There are some alarming predictions about the future, with a 2004 World Health Organization report noting: 'Unless current trends are halted or reversed, over a billion people will die from cardiovascular diseases in the first half of the 21st century.'

It's not all doom and gloom though, as the nutraceutical and functional food industry sits at the very heart of the matter of heart health. Evidence of heart-protecting ingredients mounts every day, resulting in a stack of research thicker than even the most heart-threatening, *trans*-fat and salt laden monstrosity imaginable. And cardiovascular disease (CVD) is preventable for most people—simple dietary and lifestyle changes can make a huge difference. This is where the industry can help.

As Irene Wohlfahrt explains on [page 4](#), heart health has consistently ranked as one of consumers' top five health concerns and new product launches aimed at cardiovascular health have been increasing steadily. However, consumers recognise the need for research-backed authorised health claims and are hungry for ingredients proven to help.

Phytosterols are one such ingredient. As hypercholesterolemia is rampant in the EU—Europe has the highest prevalence in the world—the potential of phytosterols in reducing the risk of cardiovascular events is particularly interesting. Starting on [page 11](#), Patrick Coppens details the results of a study into their potential in reducing CVD-attributed hospital uses costs in Europe—a cost currently estimated at €265.7 billion per year!

Of course, a healthy circulatory system and good cardiovascular health mean more than just the prevention of severe CVD, as Jim Beakey point outs on [page 17](#). Vitamin K2 plays a huge role in heart health, holding significant promise to improve the general health and wellbeing of individuals, with tremendous market potential to boot!

Everyone can benefit from making positive changes to their diet and lifestyle, and with so many natural ingredients having such heart health potential, it's time for a change of heart.



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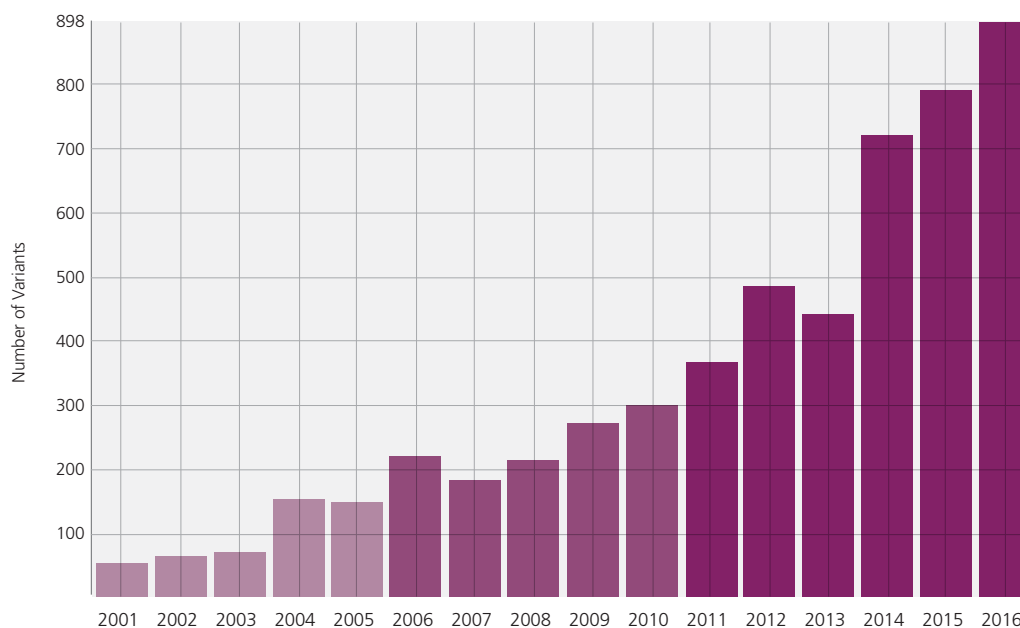


# The European Heart Health Market

by Irene Wohlfahrt

**For decades**, heart health has consistently ranked as one of consumers' top five health concerns. Statistics show cardiovascular disease (CVD)—a class of diseases including coronary artery diseases, stroke, heart failure, and others—is the leading cause of death for men and women over 65 years. Consequently, heart health is very much on the radar for health maintenance and self-medication, especially in older consumer demographics. Numerous products catering to that need exist in the supplements markets as well as the functional foods category. New product launches in these categories targeted at cardiovascular health have been increasing steadily.

**Figure 1:**  
**New product launches (food, drinks, food supplements)**  
**claimed 'cardiovascular health' in Europe 2001 - 2016**



(Source: Mintel GNPD)

Consumers interested in maintaining their heart health are generally older and statistically also overweight or suffer from a blood lipid imbalance. Due to their co-morbidities, they are reluctant to be educated on the effects of an unhealthy lifestyle and, depending on the progression of their health issues, they may or may not receive medication for blood pressure management or blood lipid management. Consumers on medication are generally not open to self-medication, since their physician is already doing it for them. The market for heart health products, therefore, lies with consumers at risk (or who consider themselves at risk) but not yet receiving medical treatment.

## Blood lipids and cholesterol

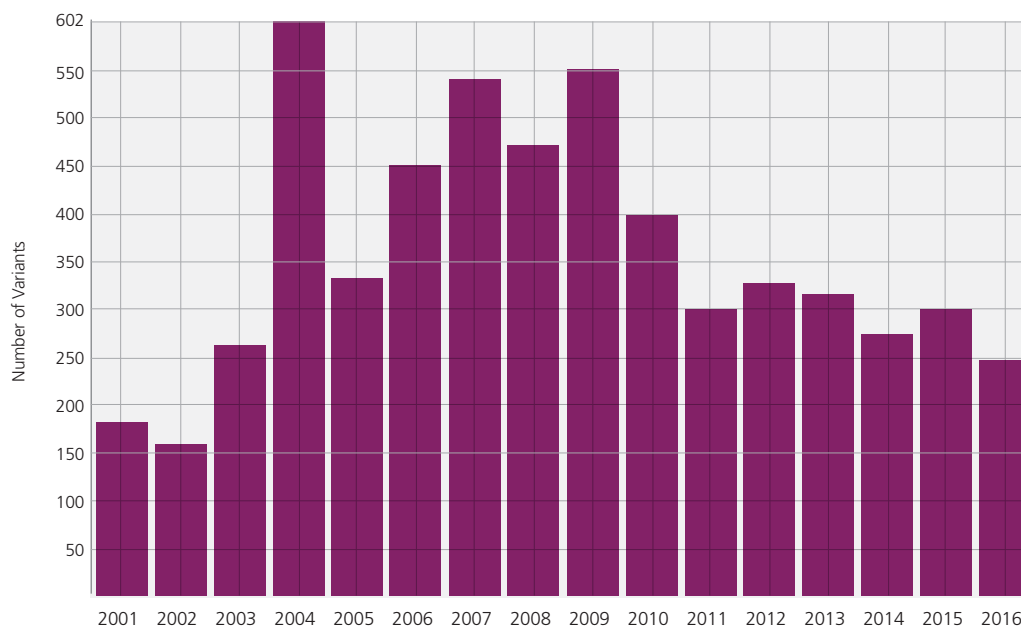
The causes for failing heart health are numerous. High on the list are high blood pressure and high cholesterol levels leading to platelet aggregation and atherosclerosis.

High cholesterol levels are determined by the volume of low-density lipoprotein (LDL) cholesterol in the blood. The high-density lipoprotein (HDL) cholesterol acts as a scavenger for LDL cholesterol and is heart-protective in that it counters the negative blocking effects of LDL cholesterol.

There are many products on the market addressing high cholesterol. One category is the so-called 'minus' claim category, in which products claim reduced, low or no cholesterol. These products thrived in Europe until 2010 but have since levelled off and even declined slightly.

**Figure 2:**

**New product launches (food, drink, supplements) featuring 'minus' cholesterol claims in Europe 2001 - 2016**



(Source: Mintel GNPD)

This may partly be due to consumer education about the merits, or lack thereof, of avoiding cholesterol uptake with the food. Since cholesterol is produced in the body, merely avoiding it in the diet does not reduce its levels in the blood, detracting from the 'minus' products' selling point.

This demonstrates catering to even top health concerns requires good sales arguments to convince consumers. Ingredients which could claim to lower cholesterol levels seem to fit this bill better. However, this is only true if the product label can claim such an effect, which means only ingredients that have received authorised health claims related to heart health realistically have good odds of surviving on the market in Europe.

## Plant Stanol Esters

One such ingredient is the group of plant stanol esters, which have received an authorised health claim relating to the risk reduction of the development of coronary heart disease (CHD). However, the use of the claim is restricted to yellow fat spreads, dairy products, mayonnaise, and salad dressings, making it unsuitable for the food supplements industry.

Benecol margarine was one of the first functional food ingredients on the heart health market in Europe. Starting in Finland, more products containing plant stanol esters soon went on to be sold globally in 30 countries. The effects of the plant stanol esters contained in Benecol's products have been proven in more than 70 clinical studies to date.

Plant stanol esters mimic cholesterol and bile in the gut, thus competing with and blocking their absorption. As a result, more bile is produced by the body, which uses up the body's cholesterol, leading to a lowering of blood levels of cholesterol. This effect is proportional to the amount of plant sterol esters taken up with the food.

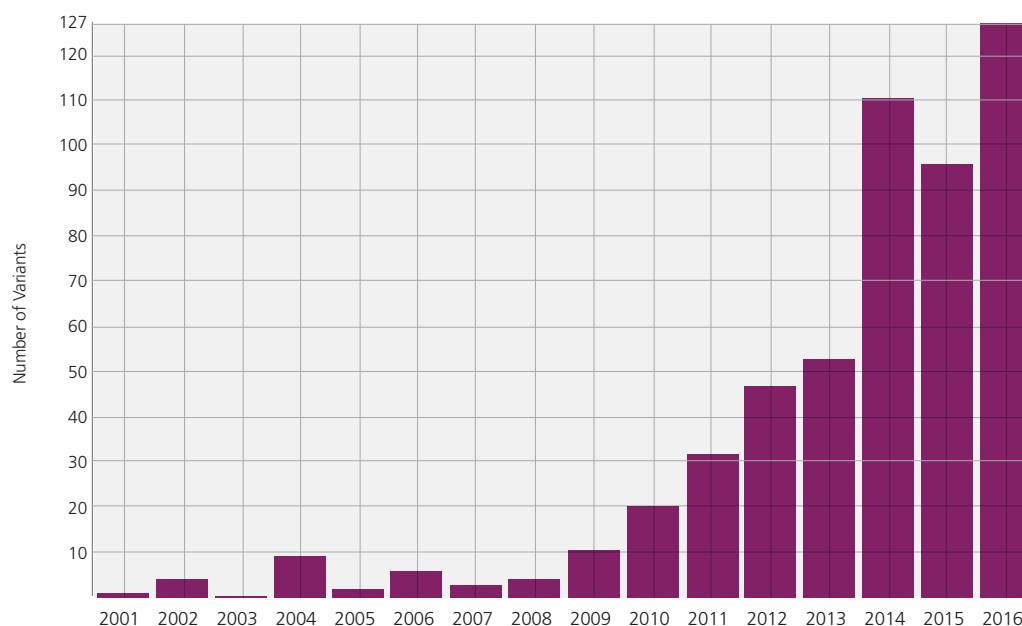
## Beta-glucans

Looking at other ingredients for which authorised health claims related to heart health can be made, beta-glucans are high on the list. They have also been proven to lower LDL cholesterol without impacting the levels of HDL cholesterol. Beta-glucan is a soluble fibre which occurs naturally in many grains including oat and barley. The cholesterol-lowering effect is achieved by consuming at least 3 g/d of beta-glucan and can be claimed for both oat and barley beta-glucans.

As a soluble fibre, beta-glucan passes through the digestive tract without being digested. During its passage, it binds cholesterol, which results in a lowered cholesterol level in the blood. As an added benefit, beta-glucans have also been found to reduce blood sugar levels. Since gaining the authorised health claim, products containing beta-glucan have been thriving.

**Figure:**

**New product launches (food, drink, supplements) containing beta-glucans in Europe 2001 - 2016**



(Source: Mintel GNPD)

The majority of these products are food products: cereals, muesli, porridge, biscuits, but also smoothies and yoghurts. Since the conditions of use for the beta-glucan health claim are prohibitive for dietary supplements—3 g of beta-glucans per day is hardly feasible, at least in tablet or capsule form—it is no surprise it is mostly food products that make use of the claim.

## Unsaturated fatty acids and omega-3

Mono- and polyunsaturated fatty acids have received authorised health claims related to cholesterol-lowering effects as well. According to the European Union's Nutrition and Health Claims Regulation (NHCR), a food that can claim to be 'high in unsaturated fat' can also claim to lower or reduce blood cholesterol, a risk factor in the development of CHD. However, the food bearing the claim can only be a fat or an oil, making it unsuitable for most dietary supplements.

The situation is better for the polyunsaturated omega-3 fatty acids: docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). They can carry a health claim relating to the contribution of the normal function of the heart—an article 31.1 claim and not a risk-reduction claim—if the food in question is at least a source of EPA and DHA and if the consumer is informed that daily intake of these fatty acids must reach 250 mg. Per the NHCR, only 40 mg of EPA and DHA per 100 g of daily dosage are required for the claim.

Omega-3 fatty acids and their health benefits have received much attention during recent years. Either animal- or plant-derived, supplements containing these unsaturated fats are soaring in most markets. The ingredient has been described as being capable of 'doing anything except start your car in the morning', and new health benefits are still being discovered.

For heart health, omega-3s are considered to have preventative rather than curing action. A recent meta-analysis showed a protective effect against cardiovascular risk in healthy adults who were suffering from hypertriglyceridemia or hyperlipidaemia, or who were overweight. Specifically, the action of omega-3 fatty acids is thought to ameliorate the effects of inflammation and oxidative stress which are suspected of lying at the heart of atherosclerotic processes.

Other studies show this anti-inflammatory effect is also beneficial for patients with existing heart diseases. However, the effect is not limited to omega-3s but can also be observed for omega-6 fatty acids and total polyunsaturated acids in the diet.

## Heart-protective vitamins

Among the vitamins, thiamine is the only one to receive a 'contributes to the normal function of the heart' claim. Thiamine deficiency is linked to many severe health issues, including with heart failure. Adequate levels of thiamine are therefore considered vital for heart health maintenance.



**Thiamine deficiency**  
**is linked to many severe health**  
**issues, including heart failure.**

Much research has gone into the role of vitamin D in the development of heart health problems. While an inverse correlation between blood levels of vitamin D and many forms of CVD has been established in Europeans and other ethnic groups, most randomised controlled trials using vitamin D supplementation show no significant effect, or no effect at all. This apparent contradiction is still being investigated; however, vitamin D's anti-inflammatory effect has been well established, as has the role of inflammation in the pathogenesis of many forms of CVD.



## Botanicals

Many ingredients yet to receive European Food Safety Authority (EFSA) approved health claims are botanicals. Science may support heart health effects for them; but, since these effects cannot be claimed on the product label, food business operators are understandably hesitant about investing into research and development for these ingredients.



## Almonds

Earlier this year, a study showed that eating almonds improves the blood status of HDL cholesterol, the 'good' cholesterol, while simultaneously improving its efficiency in reducing the 'bad' cholesterol. This effect can be observed in men and women eating approximately a handful of almonds per day from a study conducted in participants with elevated LDL cholesterol levels. The improved HDL cholesterol function could only be observed in participants with normal weight.

While it is doubtful almonds will ever be considered for serious product development in this area, this effect makes almonds a good addition to an already healthy diet.



## Sea buckthorn

Sea buckthorn contains large amounts of nutrients such as phenolics, organic acids, isorhamnetin, quercetin, kaempferol, sitosterol, carotenoids, and a number of vitamins (C, B1, B2, B12, A, K, and E). This nutrient profile has put it on the radar for many health effects related to these substances.

Recently, a meta-analysis showed sea buckthorn berries or extracts significantly improved the cholesterol blood profiles in subjects with hyperlipidaemia, but not in healthy subjects. The effect is attributed to the sea buckthorn flavonoid compounds which might have a similar action to the polyphenols contained in green and black tea.

Sea buckthorn oil also contains an omega-7 fatty acid (cis 16:1 palmitoleic acid), a mono-unsaturated fatty acid which is being investigated for possible anti-inflammatory effects. Omega-7 has enjoyed much less consumer awareness than omega-3, even though its dietary abundance is second only to oleic acid.



## Ginger

The health benefits of ginger are manifold due to the rhizome's high antioxidant content—most notably gingerols, shogaols, zingerones, and other ketones, which provide the anti-inflammatory, antioxidant, and anti-proliferative activities. A study published in 2016 indicates daily ginger consumption reduces the risk of developing hypertension by 8 percent and CHD by 13 percent in adults. This effect was achieved in the study population by a daily consumption of 2 to 4 g of ginger. The mechanism of action for this risk-reducing effect is currently not well understood. Researchers speculate it could be related to a potential



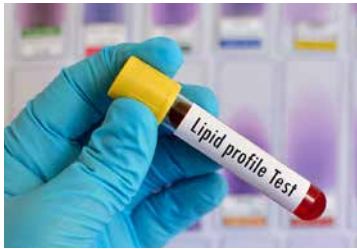


inhibitory action on angiotensin-1-converting enzyme (ACE) and prevention of peroxidation in the heart. These effects could be linked to ginger's polyphenol content.

### Cocoa

No overview of heart health and ingredients related to it would be complete without mentioning cocoa and cocoa flavanols. It is one of the few ingredients that is not a vitamin or mineral to have received an approved health claim. The proprietary health claim afforded to Barry Callebaut for 200 mg of cocoa flavanols from either cocoa beverages or dark chocolate is worded as 'contributing to normal blood flow by maintaining endothelium-dependent vasodilation'. The health claim will be proprietary for Barry Callebaut's Acticoa brand for five years from 2013. This is of interest to the consumer as well, since it adds a health benefit to a product (chocolate) which is generally seen as indulgent. However, the somewhat clumsy claim wording requires some consumer education to make the connection to heart health. Research has since shown the heart health maintaining effects of chocolate have nothing to

do with its cocoa flavanol content. In fact, increasing flavanols in chocolate even affects its taste profile, since flavanols are astringent and bitter.



### Heart health

**is a major concern for older consumers, especially for those running a higher risk of developing cardiovascular issues due to excess weight or unhealthy blood lipid profiles.**

Heart health is a major concern for older consumers, especially for those running a higher risk of developing cardiovascular issues due to excess weight or unhealthy blood lipid profiles. The market for functional foods and food supplements in Europe mainly consists of products that can claim cholesterol-lowering effects or maintenance of blood flow, since these are the only approved health claims. Other ingredients have shown heart health benefits in clinical trials, but since approved health claims are lacking, their chances on the market are limited. ●

*Irene Wohlfahrt is senior consultant at analyze & realize.*



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# Potential Healthcare Cost Savings with Phytosterol Supplementation

by Patrick Coppens

**Supplementing the diet** with specific food compounds through nutritional supplements can have considerable benefits for health. Certain interventions have been shown to effectively reduce the risk of certain chronic conditions but such studies rarely consider the healthcare cost savings of interventions.

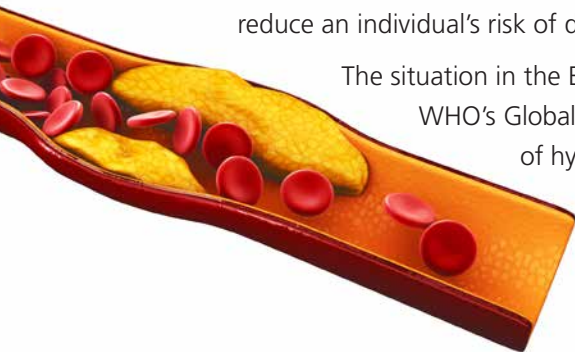
Food Supplements Europe has commissioned a number of studies with research group Frost & Sullivan to quantify the possible healthcare cost savings that could be generated through the use of specific supplements. Three studies have so far been published: one investigated the cost benefits that can be achieved by the daily use of omega-3 fatty acids in people at risk of suffering a cardiovascular event; the second addressed supplementation with calcium and vitamin D in reducing the risk of osteoporosis.

The most recent study investigated the potential healthcare cost savings from the daily use of phytosterols in people with severe hypercholesterolemia and at risk of suffering a cardiovascular event.

## The public health burden of cardiovascular disease (CVD)

Hypercholesterolemia is the presence of high total cholesterol levels in the blood, which predisposes people to a higher risk of cardiovascular disease (CVD). The presence of cholesterol—specifically, higher concentrations of low-density lipoprotein (LDL) cholesterol and lower concentrations of high-density lipoprotein (HDL) cholesterol—promotes the development of plaque in the arteries, which leads to blood flow restriction. The presence of CVD is associated with hypertension, atherosclerosis and angina pectoris and, ultimately, can lead to acute myocardial infarction, ischemic heart disease, heart failure, or cerebrovascular events. The World Health Organization (WHO) sets the cut-off level for hypercholesterolemia at 5.0 mmol/L (193 mg/dl) and for severe hypercholesterolemia at 6.2 mmol/L (240 mg/dl) of total cholesterol. Reducing cholesterol levels by dietary and pharmacological interventions is a main objective to reduce an individual's risk of developing CVD.

The situation in the European Union (EU) is particularly preoccupying. According to WHO's Global Health Observatory statistics, Europe has the highest prevalence of hypercholesterolemia in the world, at 54 percent of the total population aged 25 and older; 20 percent of the total population has severe hypercholesterolemia. It is expected the prevalence of hypercholesterolemia is greater among Europeans



aged 55 and older; however, exact figures for the entire EU are not currently available. A conservative measure of the prevalence of hypercholesterolemia was therefore adopted for the purposes of this study.

### The costs of CVD

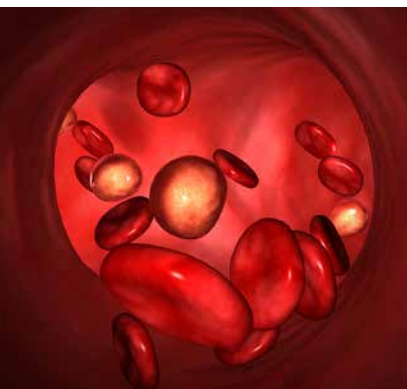
Hypercholesterolemia can ultimately result in a CVD-attributed event that requires professional medical attention and, consequently, use of hospital services, such as outpatient or office-based provider visits, hospital inpatient stays, accident and emergency department visits, prescribed medications, and home care such as home nursing and medical devices used at home. According to hospital use statistics provided by WHO's Regional Office of Europe, over 38 million CVD-attributed hospital events occurred between 2011 and 2015 in the EU among adults aged 55 and older. Thus, each individual adult aged 55 and older in the EU has a one in four chance of experiencing a CVD-attributed event requiring formal and informal health care services over the next five years. These CVD-attributed events include both primary and secondary CVD cases. In other words, a total of 38.4 million CVD-attributed hospital events are expected over the next five years (2016 to 2020) among adults aged 55 and older in the EU—24 percent of the target population will experience a CVD-attributed hospital event.



It is expected the prevalence of **hypercholesterolemia is greater among Europeans aged 55 and older**; however, exact figures for the entire EU are not currently available.

The average cost of a CVD-attributed hospital event in the EU will be €34,637 per event. This is calculated by taking total expenditure over the next five years and dividing it by the cumulative number of events. This cost calculation approach was adopted because some CVD-attributed events and the residual post treatment disease management costs may stretch beyond one year for a given event. For example, the cost of inpatient care—the expenditure for patients who require hospital admission at the beginning of the CVD-attributed event—and post-treatment informal costs such as home nurses, medical equipment for home use and lost productivity, which is typically spent over several months or years after the initial event; these are nearly equal in share of cost burden at 32.9 percent each. The cost of medications for managing CVD makes up an additional 19.1 percent of the financial burden with the remaining services contributing to CVD-attributed healthcare costs comprising a combined 15.1 percent of the cost burden, including primary care (5.7 percent), outpatient care (8.3 percent) and ambulance and emergency services (1.1 percent). Thus, the total expenditure for addressing medical events requiring a mix of hospital services for all EU adults aged 55 and older is expected to be €1,328 billion over the next 5 years, or approximately €265.7 billion per year after controlling for purchasing power parity across each country within the EU.





### The value of phytosterols in the dietary management of hypercholesterolemia

A healthy diet and lifestyle are the cornerstones of CVD prevention and should be followed regardless of concomitant drug treatment. Phytosterols are recommended for both individuals with high cholesterol levels at intermediate or low global CVD risk who do not qualify for pharmacotherapy, and as an adjunct to pharmacologic therapy in high and very high risk patients who fail to achieve LDL-cholesterol target levels on statins or are statin-intolerant.

According to the 2016 ESC/EAS Guidelines for the Management of Dyslipidemias, treatment with an intense dose of statins is recommended for male patients age 55 and older with CVD and female patients age 60 and older with CVD, or any patient with a baseline LDL cholesterol level of greater than 5 mmol/L.

Thus, current treatment guidelines state LDL cholesterol should be the primary target of therapy, since oxidized LDL particles are the main substrate for atherosclerotic plaque formation. It has been shown different methodologies of cholesterol reduction—inhibiting cholesterol absorption or cholesterol synthesis—can lead to a reduction in the risk of coronary artery disease event rate and a 1 percent reduction in LDL cholesterol reduces the risk of coronary artery disease by 1.2 to 2 percent. In a meta-analysis of the effects of a reduction LDL cholesterol concentration on the risk of coronary artery disease by Gould et al. in 2007, it was estimated a 1 mmol/L (38.7 mg/dl) reduction in LDL cholesterol provides a 26.6 percent decrease in the relative risk of experiencing any CVD-related event and a 28 percent decrease in the relative risk of a CVD-attributed death. Thus, any intervention that is shown to reduce a person's LDL cholesterol level, ought to also help reduce the odds of experiencing a costly CVD event.

One such nutrition-based regimen is the daily use of phytosterols. Phytosterols, comprising both plant sterols and plant stanols, are structurally related to cholesterol and are present in high concentrations in vegetable oils and nuts. There are many types of phytosterols, of which beta-sitosterol and campesterol are among the most abundant. Phytosterol consumption has been shown to lower LDL cholesterol levels through a mechanism of action in which phytosterols hinder cholesterol absorption in the digestive tract. Because of the strong connection to reducing cholesterol levels, the European Food Safety Authority (EFSA) has positively assessed health claims for the consumption of phytosterols as part of a diet that reduces blood cholesterol levels. EFSA confirmed LDL cholesterol can be reduced by 7 to 10 percent within two to three weeks on average if a person consumes 1.5 to 2.4 grams of phytosterols per day.

In addition, the European Atherosclerosis Society (EAS) Consensus Panel states that when plant sterols and stanols are taken at 2 g/day there is

casual significant inhibition of cholesterol absorption and this lowers LDL cholesterol levels by between 8 and 10 percent, leading the Panel to conclude phytosterols are a potent dietary option available for reducing LDL cholesterol levels.

The potential health benefits that can be derived from the daily use of phytosterols was investigated by Ras, Geleijnse, and Trautwein in 2014, which specifically evaluated the expected effects of phytosterol use across a spectrum of regimen levels on LDL cholesterol levels. In this work, a total of 124 clinical studies were systematically analysed with an average phytosterol daily usage amount across all the studies of 2.1 grams. The weighted results show the observed average reduction in LDL cholesterol levels was 8.4 percent of baseline when compared to a placebo. The strength of the correlation between the average reduction of LDL cholesterol (percent) and average phytosterol use (g/d) is very strong ( $R^2 > 0.99$ ) and implies the EFSA recommendation of 2.0 grams per day of phytosterols will yield an expected reduction of LDL cholesterol of 8.4 percent.



“ As the average person in the EU acquires 300 mg of phytosterol intake from the diet, an expected 1.7 grams should come from supplementation.

This was taken as the basis for the assessment in this study. Since adults with high LDL cholesterol levels, aged 55 and older in the EU face a 24.3 percent chance of experiencing a CVD event, the daily intake of 2 g of phytosterols can reduce this risk by 2.3 percent basis points. As the average person in the EU acquires 300 mg of phytosterol intake from the diet, an expected 1.7 grams should come from supplementation. This is an average—it should be noted the potential absolute risk reduction of a given country varies due to the level of CVD risk the citizens of these countries face. For example, adults aged 55 and older in Lithuania with high LDL cholesterol levels face a very high risk of experiencing a CVD event—consequently the potential health benefits of using a phytosterol supplement is much greater. Overall, this 2.3 percent absolute risk reduction corresponds to **170,542** possible CVD-attributed hospital events that could be avoided throughout the EU every year. Again, the likely risk reduction benefits from using phytosterols varies by EU country based on the observed CVD-attributed event rates of each country. For example, the absolute risk reduction in Lithuania is 7.3 percent and in Austria it is 4.3 percent.

### Cost-benefit ratio of phytosterol supplementation

Supplementing the diet with phytosterols also has a cost. However, it is difficult to find reliable information on the cost of phytosterol food supplements in the EU since the majority of food supplements in the market contain a mix of various components; thus, it is not feasible to find the cost of phytosterols as a single ingredient. For the few single component products that were found, the cost per gram ranged from €0.24 to €0.47. Consequently, a 1.7 gram daily regimen would cost an average of €0.56, or approximately €204.54 per year. This price

was weighted by each country's purchasing power parity ratio from the World Bank to best represent the expected variance in phytosterol prices observed in other EU markets. Accordingly, the cost of phytosterol use required to realise the expected benefits by the total target population of all adults aged 55 and older with severe hypercholesterolemia (>6.2 mmol/L) at risk of experiencing a CVD-attributed medical events per year is expected to be €1.213 billion per year.

Given the annual average cost per person for a CVD-related event (€34,637) and the 170,542 possible of avoidable CVD-attributed events in the entire target population per year, the total potential avoidable hospital use cost for all EU adults over the age of 55 with hypercholesterolemia would average €5.30 billion per year. Cyprus has the lowest potential savings (€1.2 million per year) while Germany has the highest at €2.2 billion in avoided hospital event costs per year.

Taking into account the costs of supplementation, the total net benefit for the entire EU target population of adults aged 55 and older with severe hypercholesterolemia is €4.09 billion per year. This means that for every €1 spent on a phytosterol daily regimen, there would be a certainty equivalent return to the primary payers of healthcare costs, which include governments and insurance companies, of €4.37 to society in the form of avoided healthcare expenditures attributed to CVD.

In fact, all 28 EU countries have benefit cost ratios greater than €1, which is an indication of phytosterols' cost effectiveness. The greatest net benefits are found in Germany, where an expected annualised net benefit from avoided CVD-attributed healthcare costs is €1.92 billion per year. Germany is followed by France and Italy with €468.5 million and €402.2 million in per year in total net benefits, respectively.

Overall, the yearly benefit per potential user (all adults aged 55 and older with severe hypercholesterolemia) is expected to be €170.46 per user. The greatest benefit per user was found to be in Ireland (€379 per target user per year) which is likely due to this country having a relatively high cost of care for CVD, after adjusting for purchasing power parity. On the other hand, the net benefits per person in Cyprus and Hungary have small, yet still positive, benefits per person due to lower healthcare cost burdens even after adjusting for purchasing power parity. It should be noted this does not mean that these countries would not benefit from using phytosterols daily, because these countries are still avoiding a significant number of CVD-attributed events that are directly attributed to lower productivity, higher healthcare costs, and a lower quality of life.



In conclusion, this study demonstrates the use of phytosterols can potentially reduce CVD-attributed hospital usage costs in the EU among those at a high risk of experiencing a costly, CVD-attributed event by €26.5 billion over the next five years. This has the potential to have a significant impact on a country's public healthcare cost budget.

However, the most significant impact affects all the people suffering from hypercholesterolemia, by avoiding 170,542 possible CVD-attributed hospital events every year. ●

*Patrick Coppens is director of scientific and regulatory affairs at Food Supplements Europe.*

# Health Link smoothies with EFSA nutritional claims



**The core of our smoothie is a balanced combination of flax protein, chia seeds and crushed apple with peel. Together they help lower level of cholesterol, support proper bowel function and provide a great source of Omega-3 fatty acids, protein and fiber.**

Flax protein is obtained from flaxseeds, which are known as a heart-healthy food, since they contain high amounts of Omega-3 fatty acids, fiber and lignans, which are linked to heart health.

All these nutritional components have effects on reduction of low density lipoprotein (LDL) cholesterol level, blood pressure and other cardiovascular diseases (CVD). Chia seeds contained in smoothies have also been shown to improve blood pressure, and may also increase level of healthy cholesterol in the body.

Our smoothies are high in omega 3 fatty acid (alpha linolenic acid (ALA)). A great deal of clinical evidence suggests that higher intake of omega-3 fats in a diet is associated with reductions of several CVD. Research shows that high intakes of ALA along with fibre, lignans and other antioxidants, can reduce blood cholesterol and can help reduce risk factors for heart disease, including high blood pressure. Researchers also found out, that omega-3 fatty acids intake is effective in preventing

hardening of the arteries, irregular heartbeat and heart disease, and in helping to prevent heart attacks.

## You can use following EFSA nutrition claims:

- High in Omega-3 fatty acids
- High in protein
- High in fibre

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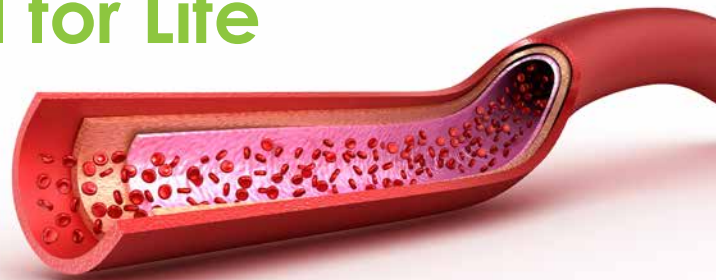
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# Vitamin K2 – Vital for Life and Wellness

by Jim Beakey



**A healthy circulatory system** and good cardiovascular health mean more than just the prevention of severe cardiovascular disease (CVD). We all benefit from good circulatory health—clean, flexible arteries and vessels that can deliver nutrient-rich blood when and where we need it and can also expand outward to meet the increased blood flow needs brought about by physical activity. Whether for senior league football, keeping pace with the kids, or just taking in the groceries—our bodies demand oxygen in response to physical activity.

Vitamin K2 plays a vital role in the prevention and reversal of arterial hardening and stiffening—a condition that constricts blood flow in the circulatory system and forces the heart to work harder. In high-risk populations, this reduces cardiovascular disease (CVD) risk. Even healthy children and teens, however, can have some degree of arterial calcification, and this condition becomes relatively common at older ages. Studies also show K2 can increase the performance of well-trained athletes.

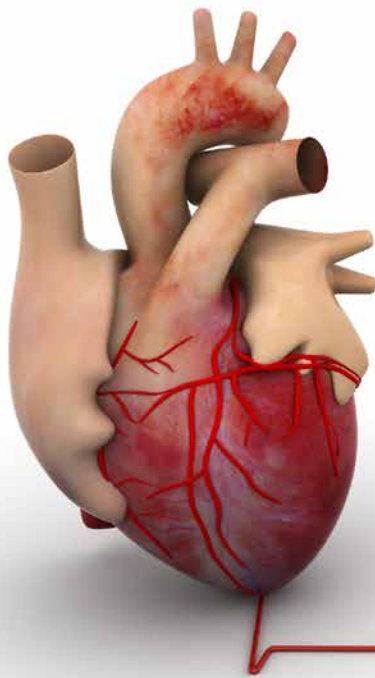
## The heart and circulatory system – fuel for living

Oxygen is a nutrient. It provides muscles and tissues the energy required to do work. When we exert ourselves, whether up the stairs or across the finish line, our bodies require more oxygen. A healthy heart and clean, flexible circulatory system can adjust to the temporary requirements of increased physical activity, pumping oxygen-rich blood to where it is needed. Calcium, however, can interfere with this process. Though critical for healthy bones, calcium has a downside as when levels are too high in the bloodstream, it can be deposited in arteries and vessels in the form of calcium plaques— at its worst, this is a predictor of cardiovascular disease<sup>1</sup>. Studies show, however, that calcification and stiffening happens in a gradual progression which can occur over decades. The early signs of arterial calcification have been observed in otherwise healthy children, and studies have reported calcium deposits in the arterial wall affect nearly 30 percent of Americans over the age of 45<sup>2</sup>, and commonly increase with age<sup>3</sup>.



**Studies** have reported calcium deposits in the arterial wall affect nearly **30 percent of Americans over the age of 45**, and commonly increase with age.

This gradual calcifying process means long before someone might enter the CVD risk zone, there is a reasonable possibility they may have some degree of circulatory system calcification.



This results in a stiffening of arteries and vessels, where they begin to lose their flexibility. These arteries and vessels begin to lose their ability to widen and expand outward in response to physical activity when the body needs to pump more blood to tissues. As a result, less oxygen is available to muscles, tissues and other systems and the heart must work harder to push blood through the rigid, reduced diameter vessels, which may be perceived as a decrease in stamina. Having less stamina may affect the ability to complete certain everyday activities.

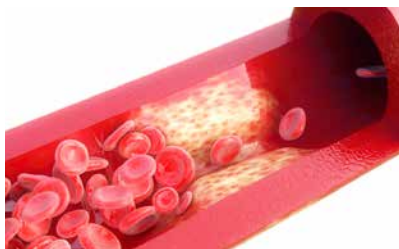
### The wellness vitamin

Vitamin K2's role in promoting life-long wellness starts early. K2 activates osteocalcin enzymes which incorporate calcium into bone. Without K2, calcium does not function optimally in the body—starting when the body is developing in-utero, K2 helps ensure healthy bone formation.

Throughout life, vitamin K2 helps build strong bones, making bodies sturdy and resilient, and protecting against bone diseases such as osteoporosis.

K2 also activates a second enzyme which plays a critical role in circulatory system health—matrix Gla protein (MGP), a calcium-binding protein<sup>4</sup>. Once activated, MGP binds excess, free-floating calcium in the blood and prevents it from being deposited in the circulatory system<sup>5</sup>. Calcium-free arteries and vessels can remain soft, flexible, and ready to adapt to the increased oxygen and blood flow needs triggered by physical activity.

Several studies support this clear correlation between K2 and arterial calcification. High blood levels of non-activated MGP (dp-ucMGP) are correlated with both low vitamin K status and vascular calcification. In healthy adults, non-activated MGP levels correlate with age<sup>5</sup>, and higher levels of non-activated MGP are observed in people at risk for vascular calcification—because of diseases that have a high correlation with calcification. Non-activated MGP is inversely correlated with poor dietary vitamin K intake, and non-activated MGP and lower CVD survival rates also demonstrate the importance of activated MGP in preventing vascular calcification<sup>6</sup>. Further, in a study of 577 older individuals, non-activated MGP was associated with increased risk of cardiovascular disease and attributed to low vitamin K status<sup>7</sup>. In summary, these studies demonstrate high levels of non-activated MGP correlate with vascular calcification.



**High blood levels of non-activated MGP (dp-ucMGP) are correlated with both **low vitamin K status** and **vascular calcification**.**

On the other hand, studies have shown vitamin K2 supplementation produces a significant decrease in non-activated MGP in healthy adults<sup>8-10</sup>. Further, vitamin K2 in doses of 90 µg and higher significantly improve the carboxylation (activation) of MGP in healthy adults. Finally, one

study showed after intake of vitamin K2 MK-7 in doses close to the recommended daily allowance (RDA of 90 µg and above), levels of activated MGP increased significantly<sup>11</sup>.

### Improving wellness and quality of life

Vitamin K2 activates the MGP proteins which bind excess calcium to prevent calcification, and research has shown it can even help to reverse calcification. It could therefore support the restoration of flexibility to vessels and arteries and help improve the body's ability to circulate blood and transport oxygen. This would contribute to future wellness and wellbeing by increasing the body's capacity to respond to physical activity.

Two large studies demonstrate the preventative role of vitamin K2. The Rotterdam study of over 4,800 men and women demonstrated diets high in vitamin K2 dramatically reduced the risk of CVD and mortality<sup>12</sup>. Another study of over 16,000 demonstrated an inverse correlation between intake of K2 and the risk of coronary heart disease, with a mortality risk reduction of 9 percent for each extra 10 µg/day K2 intake<sup>13</sup>.

The 2015 Knapen study, however, provides the strongest evidence for the reversal of existing calcification. This study showed high intake of vitamin K2 MK-7 was linked to reduced arterial calcification, and after three years, existing arterial stiffness decreased in the test group, but increased in the placebo group<sup>14</sup>.

While many K2 studies have been conducted with average healthy, elderly or diseased populations, studies on healthier subjects are beginning. A 2017 study demonstrated a 12 percent performance increase among highly trained athletes following just eight weeks of K2 MK-7 supplementation<sup>16</sup>. This increase is notable given the baseline measures for trained athletes were likely much higher than for an average person, making measurable differences more difficult to discriminate. While the mechanism of this improvement needs further investigation, this study might provide the best evidence to date that vitamin K2 could improve wellness and wellbeing for average people.

### A tremendous market opportunity

K2 is one of a handful of essential vitamins, and though identified decades ago, its importance to bone and heart health has only recently been clarified. Most western diets are considered K2 deficient<sup>17</sup> as while K2 is present in some meats, cheeses and fermented foods, one theory is that societal industrialisation—including changes in food preparation, storage, and livestock management—has reduced the amount of K2 in our diets.

K2's biggest commercial advantage, however, is its wide applicability to different consumer and market categories. Vitamin K2 is needed by both men and women throughout all stages of life—from childhood to teen years, adulthood to senior years. Children need K2 for healthy bone formation, teens during the growth-spurt years, and both genders benefit from K2's cardiovascular and circulatory health benefits, although women especially need to build a high peak bone mass to prevent bone diseases later in life.

A 2017 study demonstrated a **12% performance increase** among highly trained athletes following just eight weeks of K2 MK-7 supplementation.



A dietary deficiency combined with wide product and consumer applicability translates to tremendous market potential. The large heart health and bone health market categories are natural targets for vitamin K2. Extension categories which incorporate bone and heart health are also opportunities for K2 upgrade—the healthy ageing, wellness, and women’s health categories are all natural fits for K2. Finally, K2 holds significant promise for the sports nutrition and active lifestyles categories. In these categories, K2 will likely break ground as food fortification in dairy products like milk, yogurt and probiotic drinks, as well as sports nutrition drinks and bars.



### K2 wellness formulations

Because K2 targets bone health, existing products containing vitamin D3 or calcium are natural candidates for K2 upgrade. Vitamin D3 helps absorb calcium into the bloodstream, and K2 activates the osteocalcin enzymes that put the calcium into bone. Calcium and D3 represent two of the top five dietary supplements ingredients by market size, foreshadowing this enormous potential.

K2’s circulatory system benefits open up a wider range of supportive co-ingredients. L-arginine, B-complex vitamins and compounds like resveratrol, the foundation of the Mediterranean diet, all provide synergistic cardiovascular benefits in formulation. Omega-3s and magnesium provide significant heart and circulatory health benefits and represent two more of the top five ingredients by market size.

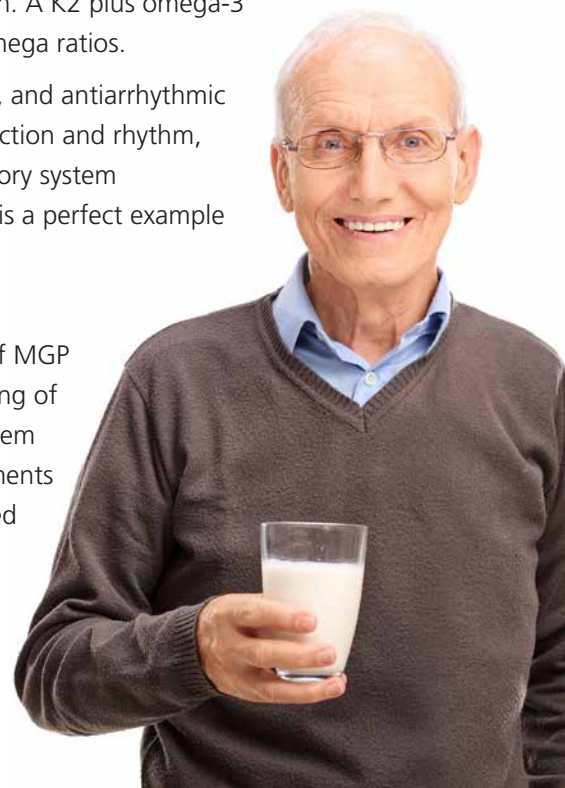
Omega-3 fatty acids are polyunsaturated fatty acids important for cellular health. The body needs both omega-3 and omega-6 polyunsaturated fatty acids, however, western diets are typically high in omega-6 (derived from processed foods, vegetable oils, and soybeans) and low in omega-3 (from fish and other seafood). As a result, the ratio between omega-3 and omega-6 can become imbalanced, negatively affecting heart health. A K2 plus omega-3 product targets heart health by balancing both the calcium and omega ratios.

Magnesium is an essential mineral with muscle-relaxing, laxative, and antiarrhythmic properties. One physiological effect is the regulation of cardiac function and rhythm, and regulation of the vascular muscular tone – helping the circulatory system maintain flexibility. A K2, magnesium, and vitamin B1 formulation is a perfect example of a product to promote wellness and wellbeing.

### The K2 conclusion

K2’s circulatory system benefits produced through its activation of MGP hold significant promise to improve the general health and wellbeing of healthy, active individuals. K2 prevents and reverses circulatory system stiffness, allowing the body to meet the increased oxygen requirements associated with physical activity. Stamina improvements experienced in athletic or daily-life activities may improve perceptions of overall wellness and wellbeing among healthy individuals. The K2 market potential is tremendous, whether defined by consumer segment, market category or co-ingredient in product formulation. ●

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# Takeaways for Your Business

**F**or decades, heart health has consistently ranked as one of consumers' top five health concerns and is very much on the radar for health maintenance, especially in older consumer demographics. Numerous products catering to this need exist in the supplements markets as well as the functional foods category and new product launches targeted at cardiovascular health have been increasing steadily. The causes for failing heart health are numerous, including high blood pressure and high cholesterol levels which lead to platelet aggregation and atherosclerosis.

Hypercholesterolemia is the presence of high total cholesterol levels in the blood, which predisposes people to a higher risk of cardiovascular disease (CVD). According to the World Health Organization's (WHO) Global Health Observatory statistics, Europe has the highest prevalence of hypercholesterolemia in the world, at 54 percent of the total population aged 25 and older, and 20 percent of the total European population has severe hypercholesterolemia.

Hypercholesterolemia can ultimately result in a CVD-attributed event that requires professional medical attention. Per hospital usage statistics provided by WHO, a total of 38.4 million CVD-attributed hospital events are expected between 2016 and 2020—with the average cost of such an event estimated at €34,637. The total expenditure for addressing these medical events is expected to be €1,3248 billion.

There are many products on the market addressing high cholesterol, many of which boast European Food Safety Authority (EFSA) authorised health claims. Phytosterols, comprising both plant sterols and plant stanols, mimic cholesterol and bile in the gut, competing with and blocking their absorption. The European Atherosclerosis Society Consensus Panel stated an intake of 2 g/day of plant sterols and stanols sees LDL cholesterol levels reduced by 8 to 10 percent—qualifying phytosterols as a potent dietary option for both individuals with high cholesterol levels at intermediate or low global CVD risk, as an adjunct to pharmacologic therapy in high, and very high risk patients who fail to achieve LDL-cholesterol target levels on statins or are statin-intolerant.

Other ingredients for which authorised health claims can be made include beta-glucans, mono- and polyunsaturated fatty acids—including docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA)—thiamine, vitamin D, almonds, sea buckthorn, ginger and cocoa.

While vitamin K2 is yet to receive any authorisation for claims related to heart health, studies have shown it plays a vital role in the prevention and reversal of arterial hardening and stiffening—a condition that constricts blood flow in the circulatory system, increasing the risk of CVD. Nicknamed 'the wellness vitamin', K2 activates osteocalcin enzymes which incorporate calcium into bone; without K2, calcium does not function optimally in the body—a claim for which it has EFSA authorisation. Vitamin K2 also activates a second enzyme, matric Gla protein (MGP), which binds excess calcium and prevents it from being deposited in the circulatory system, preventing calcification. While many K2 studies have been conducted with average healthy, elderly or diseased populations, studies on healthier subjects are beginning.

As most western diets are considered K2 deficient, there is great market potential for products incorporating the vitamin. The large heart health and bone health markets are natural targets, but K2 also holds significant promise for the sports nutrition and active lifestyles categories. ●



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