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**COGNITIVE HEALTH/
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origin, current trends and future prospects

Vitamin K2

... clinically validated cardiovascular protector

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We assume that poor cardiovascular health is a byproduct of getting older. To a degree, that is true. After all, the longer we have something, the more wear and tear it endures, even our bodies. But we can take strides early to make sure the heart—and all of its related entities—is protected.

That means starting healthy habits well before your physician admonishes you, including exercise, a diet that stars fruits and vegetables, reducing (or eliminating) smoking and alcohol, and taking the right supplements to bridge nutritional gaps. In the last category, Vitamin K2 as Menaquinone-7 (MK-7) plays a crucial role. The sooner you begin taking it, the better.

The Importance of Activation

Calcification contributes to vascular disease by increasing vessels' stiffness and fragility, impeding healthy blood flow to and from the heart, thus also increasing the workload on the heart.¹ Scientific studies have confirmed that the amount of calcium stored in the arteries is an indicator of one's cardiovascular health.²

Later studies confirmed that matrix Gla protein (MGP) is one of the most potent known modulators of vascular calcification.³⁻⁶ But for MGP to bind calcium—and thus keep it away from your blood vessels and arteries—it needs to be activated by Vitamin K2.

Vitamin K-dependent proteins – such as MGP – contain glutamic acid (Glu) residues. During carboxylation – when a carbon atom double-bonded to an oxygen atom and single-bonded to a hydroxyl group is introduced – Glu is transformed into gamma-carboxyglutamate (Gla) residues by the enzyme gamma-glutamyl carboxylase.

Gla binds calcium ions and ensures that calcium is deposited in the bones, where it needs to be. It keeps calcium away from the heart and the blood vessels, where it could cause damage. For all of this to happen, gamma-glutamyl carboxylase needs Vitamin K2 as MK-7, which is most effective in supplement form, to start the process.

Observing Heart-Health Potential

The Rotterdam population cohort study⁷, which looked at Vitamin K2 in a normal human population, solidified Vitamin K2's importance for cardiovascular health. Results among 4,807 healthy individuals (at the start of the study) age 55 and older, suggested a strong protective effect of the highest dietary Vitamin K2 intake on arterial calcification. The study showed a reduction in risk for cardiovascular diseases and cardiovascular disease-related deaths by as much as 50 percent for subjects who ingested more Vitamin K2. High intakes of Vitamin K2 also reduced the all-cause mortality by 25 percent.

The Prospect study included 16,057 women, and after 8 years of follow-up, Vitamin K2 was found to decrease the risk of negative coronary events by 9 percent for every 10 mcg of Vitamin K2 consumed daily. The scientists found that the strongest correlation was seen in cases of intake of the higher menaquinones (MK-7, MK-8, and MK-9). Vitamin K1 intake was not significantly related to coronary heart disease.⁸

While the data are remarkable, the Centers for Disease Control and Prevention have their own statistics: Each year, 610,000 people—or one in four—die from heart disease. Over 700,000 people have a heart attack every year. Interest in finding safe and efficacious measures to decrease these figures is paramount.⁹ Researchers and supplement manufacturers see the immense value of Vitamin K2's role in protecting the population against cardiovascular disease, particularly with the slate of recent studies.

Intervention Data Confirms Benefits

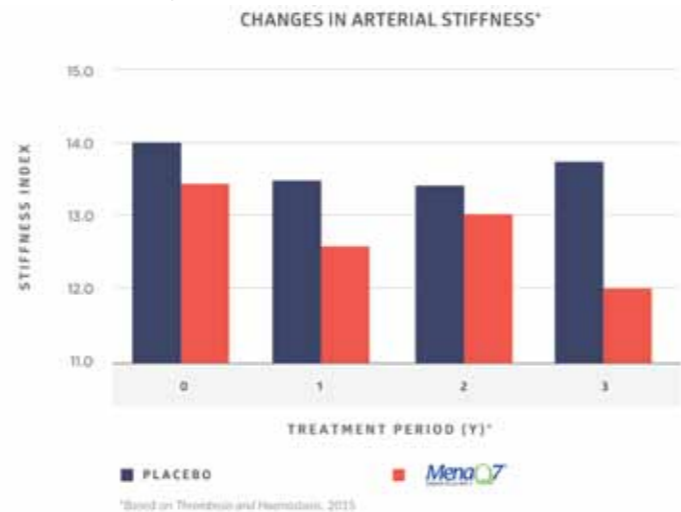
While observational data previously suggested a link between Vitamin K2 intake and cardiovascular health, an intervention trial with cardiovascular endpoints published May 2015, confirmed the association.

The VitaK research group in Maastricht, The Netherlands monitored 244 healthy post-menopausal women for three years using pulse wave velocity and ultrasound techniques as the main biological markers that were observed during the study period. The participants, 55 to 65 years old, were randomly assigned to take 180 mcg of MK-7 (MenaQ7[®] from NattoPharma ASA) daily for three years, or placebo capsules.¹⁰

The results confirmed that MenaQ7 not only inhibited development of age-related stiffening of the artery walls, but also made an unprecedented statistically significant improvement of vascular elasticity. Meaning arteries actually became more flexible.

And while this is an incredible discovery of a cardiovascular benefit of Vitamin K2 as MK-7, later last year a review paper highlighted that the effectiveness of MK-7, might actually be hindered by a common cholesterol drug therapy: Statins. A 2015 paper in *Expert Review Clinical Pharmacology* stated that statins may act as “mitochondrial toxins” with negative effects on the heart and blood vessels not only via the depletion of coenzyme Q10 (CoQ10), but also by inhibiting “the synthesis of vitamin K2, the cofactor for matrix Gla-protein activation, which in turn protects arteries from calcification.”¹¹

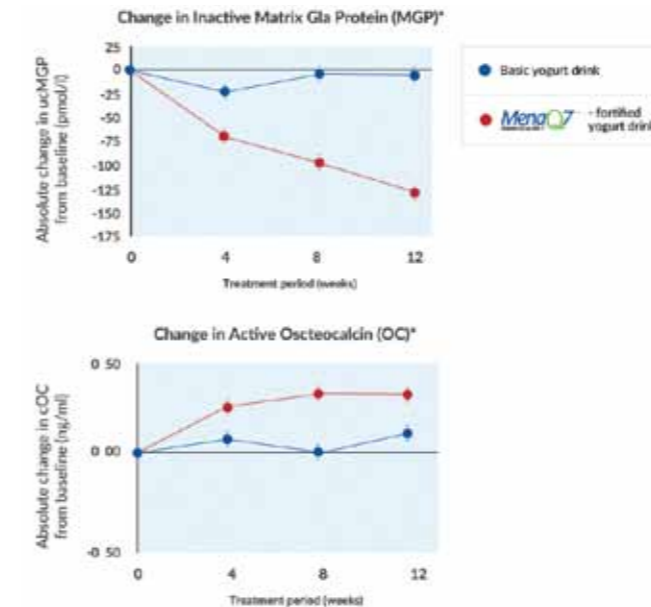
This is an important consideration, because while practitioners recommend that people on statins should take supplemental CoQ10 to offset the CoQ10-depleting effects of the medication, no such recommendation exists for Vitamin K2.



Vitamin K2 and the Food Breakthrough

Previously, the effects of increased menaquinone intake on markers of vascular health have been investigated using predominantly food supplements. Therefore, researchers sought to study the effects of a menaquinone-fortified yogurt drink (as MenaQ7[®] Vitamin K2 as MK-7) on vitamin K status and markers of vascular health in healthy men and postmenopausal women.

The MK-7-fortified yogurt drink (28 mcg) was also fortified with omega-3 polyunsaturated fatty acids, vitamin D, vitamin C, calcium, and magnesium to support vascular and/or general health. Healthy men (n=32) and postmenopausal women (n=28) with a mean age of 56 (SD 5) years received either basic or fortified yogurt drink twice per day for 12 weeks. The study showed that MK-7 was efficiently absorbed from the fortified yogurt drink. Levels of circulating MK-7 were significantly increased from 0.28 to 1.94 ng/ml. Intake of the fortified yogurt drink improved vitamin K status, as measured by significant decreases in uncarboxylated (inactive) osteocalcin and desphospho-uncarboxylated matrix Gla protein. In summary, consumption of a yogurt drink fortified with low doses of among others MK-7 for 3 months significantly improved vitamin K status in a healthy population, contributing to improved cardiovascular health.¹²



Next, the same researchers compared the fasting plasma concentrations of MK-7 (again, MenaQ7 from NattoPharma ASA) from three products: yogurt enriched with MK-7, vitamins D3 and C, magnesium, n-3 poly unsaturated fatty acids (n-3 PUFA), and fish oil (yogurt Kplus); yogurt fortified with MK-7 only (yogurt K); and soft gel capsules containing only MK-7.

The research was conducted over 42 days. The subjects were healthy men and post-menopausal women between 45 and 65 years of age. Circulating MK-7, 25-hydroxy vitamin D (25(OH) D) and markers for vitamin K status [uncarboxylated osteocalcin (ucOC) and desphospho-uncarboxylated matrix Gla-protein (dp-ucMGP)] were assessed. (Note: Uncarboxylated, or inactive, osteocalcin (ucOC) is an indicator of Vitamin K2 status. The more inactive osteocalcin—a Vitamin K-dependent protein that binds calcium to bone—you have, the lower the range of Vitamin K2.)

The increase in plasma MK-7 with the yogurt K-plus product was more pronounced than the increase in MK-7 with the capsules. However, circulating dp-ucMGP and ucOC were significantly lowered after consumption of both the yogurt products and the MK-7 capsules, reflecting vitamin K status improvement from both delivery methods.¹³

The efficacy of MK-7 in yogurt is a stunning development, because this form of Vitamin K2 is not readily available and is difficult to obtain from diet alone.

Vitamin K2, distinguished by unsaturated side chains of isoprenoid units varying in length from 1 to 14 repeats (MK-1 to MK-14), is extremely uncommon as it is predominantly microbial in origin. This can be seen in MK-7, long considered the most beneficial form of Vitamin K2. Its best food source is natto, a fermented soybean dish that is popular in some areas of Japan. In the Western world, it is mostly unavailable.

Vitamin K2's deliverability via yogurt introduces a familiar, palatable vehicle for MK-7, one that could inspire manufacturers to make a product that millions of Americans (of all ages) could enjoy.

K2 Deficiency: Consequences for Health

Recent clinical documentation demonstrates that Vitamin K2 as MK-7 is one of the most important biological activators of the protein MGP, and that a high level activated MGP will secure less stiff arteries as you grow older. Epidemiological data claims that both your risk for developing cardiovascular diseases is reduced if you have too little Vitamin K2 in your daily diet. It also is documented – and agreed upon by scientists and nutritionists – that the daily Western diet contains too little Vitamin K2.¹⁴ To that end, the only reasonable conclusion is that Vitamin K2 supplementation should be used by all health-concerned people, in order to protect themselves from developing cardiovascular diseases.

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