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VITAL HELP WITH VITAMINS

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Vitamin K2

. . . science-based bone benefits for all stages of life

By Dr. Hogne Vik, Chief Medical Officer of NattoPharma ASA, Norway

Most associate Vitamin K with aiding the blood in clotting, a Nobel Prize-winning discovery that goes back to 1929. In present day, Vitamin K – specifically Vitamin K2 – has developed a promising reputation as an effective nutrient for bone support. Even if you categorize bone health as solely an issue for the senior community – and it most certainly is *not* – the research supporting this important category represents good news for millions.

Form Matters

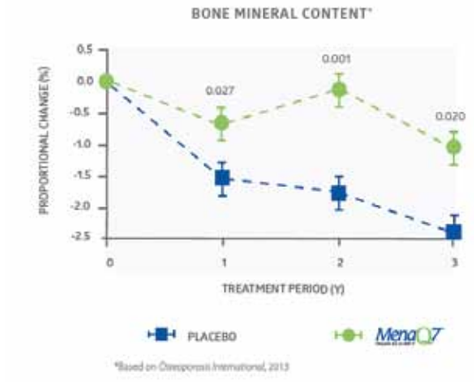
Getting the right form of Vitamin K, however, remains crucial. Vitamin K denotes a fat-soluble vitamin that occurs in two biologically active forms, phylloquinone (Vitamin K1) and menaquinone (Vitamin K2). While Vitamin K1 can be obtained through green leafy vegetables, Vitamin K2 is predominantly of microbial origin and comprises a family of molecules distinguished from K1 by unsaturated side chains of isoprenoid units varying in length from 1 to 14 repeats (e.g., menaquinone-4, menaquinone-7, etc.). These are represented by MK-4, MK-7, and so on.

The commonly recognized function of Vitamin K is as a cofactor for □-glutamylcarboxylase, an endoplasmic enzyme involved in the posttranslational carboxylation (activation) of proteins with glutamic acid (Glu) residues into □-carboxyglutamate (Gla). With the activation of glutamic acid residues on the protein substrate, a negative chemical group is formed that attracts and binds positively charged calcium.[1]

Calcium is a central element in the physiological role played by the Gla protein. Yet the body cannot properly utilize calcium without Gla proteins and Vitamin K2. This is where details become important. Vitamin K2 is responsible for the activation of osteocalcin, the protein that binds calcium to bone. Specifically, Vitamin K2 as MK-7 is the form of Vitamin K most effective in carrying out this process.

Clinical Support

A growing body of research supports this claim. A three-year study of MK-7 (MenaQ7® from NattoPharma) and 244 healthy women, published in *Osteoporosis International* in 2013, showed the first clinically statistically significant protection of the vertebrae and the hip (femoral neck) against bone loss. This was achieved with a nutritional dose of 180mcg daily of MenaQ7®. The MenaQ7® supplementation group significantly increased the circulating active osteocalcin (cOC), a well-established biomarker for bone and vitamin K status. The inactive osteocalcin (ucOC) in the MenaQ7® group, decreased with 51% +/- 21% as compared to the placebo group (+4% +/- 49%). After three years of supplementation, maintenance in both bone mineral content and bone mineral density were statistically significant in the MenaQ7® group. Moreover, bone strength was statistically improved, demonstrating therapeutic benefits for the MenaQ7® group as compared to the placebo group.[2]



Vitamin K2 as MK-7 also ensures that calcium does not deposit where it does not belong, protecting cardiovascular health. By activating another K-dependent protein, Vitamin K2 allows for the elasticity of the blood vessels and the inhibition of their calcification.

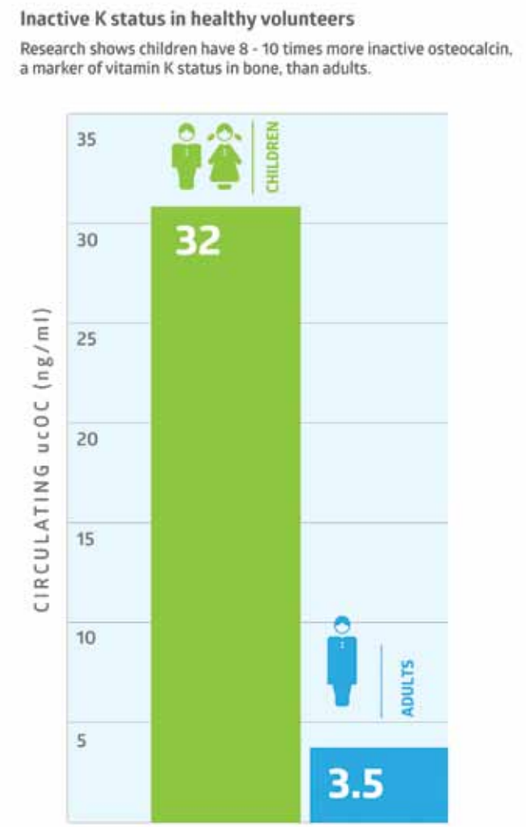
A breakthrough study published in May 2015's *Thrombosis and Haemostasis* proved just that. It monitored 244 healthy post-menopausal women for three years using pulse wave velocity and ultrasound techniques. The participants, ranging in age from 55 to 65 years old, were randomly assigned to take 180 mcg of Vitamin K2 as MK-7 (again NattoPharma's MenaQ7®) daily for three years, or placebo capsules. After three years of treatment, the Stiffness Index ß in the MK-7 group with the highest initial arterial stiffness had decreased significantly compared to the similar subpopulation in the placebo group (0.67 ± 2.78 vs +0.15 ± 2.51, respectively, p=0.018). Results confirmed that Vitamin K2 as MK-7 not only inhibited age-related stiffening of the artery walls, but also made a statistically significant improvement of vascular elasticity. [3]

Last year a study in *The Journal of Nutritional Science* further highlighted MK-7's positive effect on both bone and cardiovascular health. Researchers examined a MK-7-fortified yogurt drink (28 µg MenaQ7® PURE yogurt drink) for its effect on Vitamin K status as well as markers of vascular health. The yogurt drink 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. 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 inactive osteocaclin and MGP.[4]

Increasing Market Need for Vitamin K2

The importance MK-7's role in bone health extends beyond senior citizens. According to the American Association of Orthopaedic Surgeons, osteoporosis affects more than 200 million people worldwide. Ten million Americans have osteoporosis; another 18 million are at risk of developing the disease.[5]

The probability of developing a bone disease later in life is closely related to the amount of bone mass one accumulates before age 30, so it is essential to adopt good bone-building habits early. Up to 90% of peak bone mass is acquired by age 18 in girls and by age 20 in boys. Just a *10% increase* in bone mass is estimated to reduce the risk of osteoporotic fracture



in adult life by 50%.[6]

Vitamin K2's importance here is apparent just by reviewing basic human development. Every seven years, the entire skeleton is replaced, a process that is regulated by osteoblasts and osteoclasts. The same cells are affected by MK-7: osteoblasts produce osteocalcin, the same Vitamin K-dependent protein that binds calcium to the bone matrix. A 2014 study published in *Food & Function* revealed that healthy children have the largest tissue-specific Vitamin K deficiency – eight to 10 times more inactive osteocalcin – followed by adults 40 years and older.[7] And still more research has emphasized the importance of MK-7 supplementation: A 2009 published study indicated that improving vitamin K status in children over a two-year period resulted in stronger, denser bones. A year later the same group demonstrated that in healthy pre-pubertal children, modest supplementation with MenaQ7® Vitamin K2 as MK-7 increased osteocalcin activation.[8]

In this eight-week, double-blind, randomized, placebo-controlled trial, 45 mcg of Vitamin K2 as MK-7 (as NattoPharma's MenaQ7®) was given to healthy pre-pubertal children. The placebo group displayed no significant changes in ucOC, cOC, the ratio of ucOC to cOC, and MK-7, while those who took the Vitamin K2 supplement saw increased osteocalcin carboxylation, the 2009 *British Journal of Nutrition* study concluded.

Further, diets have worsened, and our food is not handled or grown with the care of years past. Those two factors have increased the need for supplemental Vitamin K2. A 2005 British study compared dietary intake and sources of Vitamin K in 4,599 4-year-old children born in the 1950s and 307 children in the 1990s. Dietary Vitamin K intake, the study showed, was significantly higher (P<0.001) in the 1950s (39 µg a day) compared to the 1990s (24 µg a day).[9]

The decrease in children's Vitamin K intake could help explain the increase in childhood forearm fractures. These are a common occurrence for children around puberty, possibly because children's physical activity increases while there is less cortical bone mass due to the increased calcium demand during skeletal growth. A 2003 population-based research study in Minnesota examined forearm fractures in children during four time periods from 1969 to 2001.[10]

The annual incidence rates of forearm fractures per 100,000 increased significantly from 263.3 in 1969-1971 to 322.3 in 1979-1981, and to 399.8 in 1989-1991 before leveling off at 372.9 in 1999-2001. Age-adjusted incidence rates per 100,000 were 32% greater among males in 1999-2001 compared with 1969-1971 (P =0.01), and 56% greater among females in the same time periods (P<0.001). Another study conducted in Denmark showed that the fracture rate increased by 33% in girls and 5% in boys between 1975 to 1979 and 1985.[11]

Conclusion

Vitamin K2 has been well documented for its important role of physiological calcium-metabolism throughout life -- we need sufficient K2 to secure healthy skeletal foundation during childhood; we need K2 to secure healthy, strong bone during our active, adult life; and we need vitamin K2 to inhibit loss of bone mass and strength during our senior years. As most published estimates of vitamin K2 content and intake in diets from Europe, U.S., and Asia conclude with that we are not consuming sufficient vitamin K2, supplementation of this important nutrient presents a viable alternative.

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