



suPrimo ESSENTIALS

PRIMO ESSENTIALS VITAMIN K2

CLINICAL APPLICATIONS

- SUPPORTS HEALTHY BLOOD CIRCULATION
- PROMOTES OPTIMAL BONE HEALTH AND PROPER CALCIUM STORAGE

- SUPPORTS CARDIOVASCULAR HEALTH AND ARTERIAL ELASTICITY
- BOOSTS IMMUNE FUNCTION

Emerging research highlights the importance of optimal intake of vitamin K and its critical role in maintaining bone and cardiovascular health. Composed of a group of naturally occurring and structurally similar, fat-soluble vitamins, vitamin K is required for the proper utilization of calcium and helps to bind newly absorbed calcium to the bone matrix. Vitamin K helps maintain bone mineral density by decreasing the activity of osteoclasts, cells which break down bone.¹ It also provides critical cardiovascular protection by activating matrix Gla protein (MGP), a potent inhibitor of circulatory calcification.^{2,3} Current research has found high concentration supplementation, at 180 µg/day, results in improved clinical results compared to lower-dose supplementation.⁴ Vitamin K2 180 mcg provides an optimal dose of soy-free vitamin K2 delivered in the MK-7 form for optimal support of bone, cardiovascular and immune health.

Overview

Calcium and vitamin D are important mediators in bone growth, but vitamin K plays an equally important role. The synthesis of bone growth is dependent on vitamin K, through its carboxylation of osteocalcin, a protein secreted by osteoblasts.⁵ Osteocalcin guides calcium into bones and prevents its absorption into organs, joint spaces and arteries. Vitamin K occurs in three main forms: K1 (phylloquinone), found primarily in the liver, naturally occurs in green leafy vegetables and is considered to be the main dietary source;⁶ K2 (menaquinone), which is a group name for a family of related compounds differentiated by their side chains;⁷ and K3 (menadione), which does not have vitamin K activity.⁸ MK-4 and MK-7 are the two subclasses of K2 most widely studied for

their role in bone and cardiovascular health. MK-4 is primarily a metabolic byproduct of K1 while MK-7 is found in small quantities in liver mitochondria and other tissues.⁷ The MK-7 form is substantially more active, has a longer half-life and accumulates to higher concentrations in serum than vitamin K1.^{4,9} The different degrees of bioavailability between K1 and K2 are due to differences in structure. The long side-chain of vitamin K2 (specifically MK-7) allows it to bind with fat particles in circulation. This process then allows easier facilitation to soft tissue, bones and arteries. More recently, research has shown that doses of 180 mcg of MK-7 provide greater results when supporting both bone and cardiovascular health.⁴

Vitamin K Depletion†

Although most people consume adequate dietary levels/amounts of vitamin K to maintain sufficient blood clotting, most do not consume enough MK-7 to meet cardiovascular and bone health needs. Compromised intestinal absorption can also lead to insufficient K2 levels leaving calcium available to be exported out of bone and into other tissues. Other medications such as antibiotics, cholesterol-lowering medications and laxatives have also been found to contribute to a deficiency of vitamin K.^{10,11}

Bone Health†

Supplementation of K2 has repeatedly been shown to help maintain bone density and strength among women.¹² Research from Japanese populations has found superior bone health among women who more frequently consumed MK-7 rich nattō than those who did not.¹³ The positive effect of K2 on bone health is also evident among healthy children, among whom modest supplementation with MK-7 has been shown to

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increase osteocalcin carboxylation.⁹ In a randomized, placebo-controlled trial, 180 mcg of MK-7 or placebo were given to 244 healthy post-menopausal women over the course of three years. After at least two years, statistically significant benefits were seen in vertebrae, hip and femoral neck.¹⁴ Another ground-breaking randomized, placebo-controlled trial gave 244 women, aged 55-65, 180 mcg of vitamin K2 or placebo. The study found that those given the K2 were significantly better able to maintain their osteoclast to osteoblast ratio. Furthermore, levels of circulating osteocalcin, a marker related to tissue calcification in the body, were reduced by 50% among women taking K2 versus a 4% increase among the placebo group after two and three years.⁴

Cardiovascular Health and Blood Sugar Balance[†]

Vitamin K also plays a key role in supporting the cardiovascular system and healthy blood sugar balance. In a large population study, those who consumed high amounts of K2 had significantly improved cardiovascular markers compared to those given vitamin K1.¹⁵ A cohort of over 16,000 women also linked higher intake of K2 with better maintenance of cardiovascular health.¹⁶ Studies have also shown vitamin K to support healthy blood sugar metabolism.^{17, 18} Doses of 180 mcg of K2 have been shown to have a positive effect on arterial and vascular elasticity. Additionally, 180 mcg of K2 given over two to three years has been shown to help maintain soft tissue health and vascular elasticity in healthy adult subjects.¹⁹ The same amount of MK-7 was also found to impart substantial benefits in arterial plasticity and blood vessel elasticity in healthy women, which had previously been only with “pharmacological doses” of synthetic vitamin K of up to 4,500 mcg daily.¹⁴

Triage Theory[†]

The Triage Theory states that in the face of nutrient inadequacies, nature ensures short term survival of a cell is protected at the expense of long term consequences.^{20,21} Vitamin K is an excellent example of this theory. Hypothetically, a short term deficiency in vitamin K would lead to a reduction in blood clotting. This direct threat to survival does not happen, as the body uses its metabolic reserve of vitamin K to ensure immediate needs are met. If continued, this dip into reserve leads to a long-term deficiency in vitamin K. Though not directly threatening immediate survival, long-term deficiencies are linked to bone fragility, arterial calcification and genomic instability. These issues are related to a loss of vitamin K-dependent proteins not required for short-term survival, nevertheless presenting long-term health challenges.²⁰

Directions

1 capsule per day or as recommended by your health care professional.

Does Not Contain

Wheat, gluten, dairy products, fish, shellfish, peanuts, tree nuts, egg, artificial colors, artificial sweeteners or preservatives.

Cautions

Do not consume this product if you are pregnant or nursing.

Supplement Facts ^{v2}		
Serving Size 1 Capsule		
Servings Per Container 60		
1 capsule contains	Amount Per Serving	% Daily Value
Vitamin K (K2 as Menaquinone-7 (MK-7, MenaQ7 [®] PRO))	180 mcg	150%

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References

1. Weber P. Management of osteoporosis: is there a role for vitamin K? International journal for vitamin and nutrition research *Internationale Zeitschrift für Vitamin-und Ernährungsforschung Journal international de vitaminologie et de nutrition*. 1996;67:350-356.
2. Cranenburg EC, Vermeer C, Koos R, Boumans M-L, Hackeng T-M, Bouwman FG, Kwajitaal M, Brandenburg VM, Ketteler M and Schurgers LJ. The circulating inactive form of matrix Gla Protein (ucMGP) as a biomarker for cardiovascular calcification. *Journal of vascular research*. 2008;45:427-436.
3. Furie B and Furie BC. The molecular basis of blood coagulation. *Cell*. 1988;53:505-518.
4. Knapen M, Drummen N, Smit E, Vermeer C and Theuwissen E. Three-year low-dose menaquinone-7 supplementation helps decrease bone loss in healthy postmenopausal women. *Osteoporosis International*. 2013;24:2499-2507.
5. Gundberg CM, Nieman SD, Abrams S and Rosen H. Vitamin K status and bone health: An analysis of methods for determination of undercarboxylated osteocalcin 1. *The Journal of Clinical Endocrinology & Metabolism*. 1998;83:3258-3266.
6. Booth SL, Sadowski JA and Pennington JA. Phylloquinone (vitamin K1) content of foods in the US Food and Drug Administration's total diet study. *Journal of agricultural and food chemistry*. 1995;43:1574-1579.
7. Shearer MJ and Newman P. Metabolism and cell biology of vitamin K. *Thromb Haemost*. 2008;100:530-547.
8. Buitenhuis HC, Soute BA and Vermeer C. Comparison of the vitamins K 1, K 2 and K 3 as cofactors for the hepatic vitamin K-dependent carboxylase. *Biochimica et Biophysica Acta (BBA)-General Subjects*. 1990;1034:170-175.
9. Van Summeren MJ, Braam LA, Lilien MR, Schurgers LJ, Kuis W and Vermeer C. The effect of menaquinone-7 (vitamin K 2) supplementation on osteocalcin carboxylation in healthy prepubertal children. *British journal of nutrition*. 2009;102:1171-1178.
10. Shirakawa H, Komai M and Kimura S. Antibiotic-induced vitamin K deficiency and the role of the presence of intestinal flora. *International journal for vitamin and nutrition research Internationale Zeitschrift für Vitamin-und Ernährungsforschung Journal international de vitaminologie et de nutrition*. 1989;60:245-251.
11. Hirota Y, Nakagawa K, Sawada N, Okuda N, Suhara Y, Uchino Y, Kimoto T, Funahashi N, Kamao M and Tsugawa N. Functional Characterization of the Vitamin K 2 Biosynthetic Enzyme UBIAD1. 2015.
12. Knapen M, Schurgers L and Vermeer C. Vitamin K2 supplementation improves hip bone geometry and bone strength indices in postmenopausal women. *Osteoporosis international*. 2007;18:963-972.
13. Kaneki M, Hedges SJ, Hosoi T, Fujiwara S, Lyons A, Ishida N, Nakagawa M, Takechi M, Sano Y and Mizuno Y. Japanese fermented soybean food as the major determinant of the large geographic difference in circulating levels of vitamin K2: possible implications for hip-fracture risk. *Nutrition*. 2001;17:315-321.
14. Plaza SM and Lamson DW. Vitamin K2 in bone metabolism and osteoporosis. *Alternative medicine review: a journal of clinical therapeutic*. 2005;10:24-35.
15. Geleijnse JM, Vermeer C, Grobbee DE, Schurgers LJ, Knapen MH, Van Der Meer IM, Hofman A and Witteman JC. Dietary intake of menaquinone is associated with a reduced risk of coronary heart disease: the Rotterdam Study. *The Journal of nutrition*. 2004;134:3100-3105.
16. Gast G-CM, de Roos NM, Sluijs vdl, Bots ML, Beulens JW, Geleijnse JM, Witteman JC, Grobbee DE, Peeters PH and van der Schouw YT. A high menaquinone intake reduces the incidence of coronary heart disease. *Nutrition, Metabolism and Cardiovascular Diseases*. 2009;19:504-510.
17. Beulens JW, Grobbee DE, Sluijs I, Spijkerman AM and Van Der Schouw YT. Dietary phylloquinone and menaquinones intakes and risk of type 2 diabetes. *Diabetes Care*. 2010;33:1699-1705.
18. Choi HJ, Yu J, Choi H, An JH, Kim SW, Park KS, Jang HC, Kim SY and Shin CS. Vitamin K2 supplementation improves insulin sensitivity via osteocalcin metabolism: a placebo-controlled trial. *Diabetes Care*. 2011;34:e147-e147.
19. Theuwissen E, Smit E and Vermeer C. The role of vitamin K in soft-tissue calcification. *Advances in Nutrition: An International Review Journal*. 2012;3:166-173.
20. McCann JC and Ames BN. Vitamin K, an example of triage theory: is micronutrient inadequacy linked to diseases of aging? *The American journal of clinical nutrition*. 2009;90:889-907.
21. Ames BN. Low micronutrient intake may accelerate the degenerative diseases of aging through allocation of scarce micronutrients by triage. *Proceedings of the National Academy of Sciences*. 2006;103:17589-17594.