

Tri-K: The Synergy of Three Forms of Vitamin K



New Awareness for Many Important Roles of Vitamin K—By Cristiana Paul, M.S.

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A newly defined vitamin K deficiency may impair many metabolic functions.[18] There is a paradigm shift in our understanding of the physiological role of vitamin K that now goes well beyond that of blood clotting.

Vitamin K1 and/or K2 supplementation studies have suggested that it may produce the following benefits:

- Increased BMD (bone mineral density) (by maximizing calcium deposition in the bone)[10, 11, 22, 48]
- Reduced risk of fracture (by improving bone architecture) [5,6, 22]
- Inhibition of bone resorption (by reducing formation of osteoclasts, the cells that break down bone) [22]
- Increased peak bone mass during development [55, 56, 57]
- Enhancement of tooth mineralization [59]
- Prevention and reversal of arterial calcification, stiffness and possibly hypertension [10, 17, 68, 73, 74].
- Reduced arterial plaque progression, arterial wall (intima) thickening and lipid peroxidation [50]
- Reduced inflammation (PGE2, COX-2 [3], IL-6 [30]) and symptom relief in rheumatoid arthritis [20]
- Increased apoptosis (death) of cancer cells, as in myeloproliferative diseases including leukemia [34]
- Reduced risk of developing hepatocarcinoma arising from Hepatitis C [34]
- Brain and nerve myelination support [38] (maintenance of normal lipid sulfatide metabolism)
- Reduced severity of cystic fibrosis [85] (1 mg vitamin K1 was used to compensate for carboxylation defects)

Vitamin K deficiency may have the following consequences:

- Increased risk of calcification inside arterial walls and heart valves, especially when supplementing with vitamin D (Vitamin D increases the absorption and transport of calcium, which in turn requires adequate amounts of vitamin K to activate the MGP proteins that reject calcium deposition in soft tissues, including arteries) [49], increased risk of hypertension (calcification of arterial muscle elastic fibers [73, 74])
- Increased risk of calcification of varicose veins [37], kidney and muscle [42] and other soft tissues.
- Increased cartilage calcification [32], altered cartilage maturation (excessive growth plate mineralization) [33, 62, 65], contribution to the age-related degeneration of the intervertebral disks (increased calcified/uncalcified cartilage ratio) [61, 66]
- Increased osteoarthritis disease activity [31]
- Increased risk of hemorrhage (i.e., excessive menstrual, gum or nose bleeding) [92]
- Impaired insulin secretion [21]
- Increased risk of kidney stone formation [35, 36]
- Increased skin collagen breakdown (vitamin K dependent proteins are found in dermis and epidermis)[51, 52]
- Suboptimal energy production [95], 10% reduction in muscle creatine kinase, 20% reduction in intestinal mucosa alkaline phosphatase may be due to structural mitochondrial alteration when deficient in vitamin K.

Optimal dose and administration of vitamin K

Research has been accumulating for more than 10 years that suggests a need for redefining the optimal recommended intake of vitamin K to a higher level than the current Adequate Intake(AI) of 90/120mcg (women/men). [48]. The best evidence to date for an optimal intake of vitamin K suggests 1-2 mg K1/day [24]. Aging, poor conversion of K1 to K2, genetic polymorphisms affecting vitamin K activation or action [87], and severe vitamin K related conditions, may require higher doses of K1 and additional K2 [23, 44, 75].

Most patients may need only one capsule of Tri-K per day, taken with a fatty meal, if their diet and other supplements do not provide an adequate amount of vitamin K. Tri-K may be used in conjunction with other DFH products that contain significant amounts of vitamin K: OsteoForce (1 mg K1), Vitamin D Synergy (200 mcg K1), Vitamin D Supreme (500 mcg K1+50 mcg K2) and/or PaleoGreens (contains a variable amount of vitamin K because it is composed of extracts of vitamin K-containing vegetables).

Supplement Facts

Serving Size 1 capsule
Servings Per Container 60

Amount Per Serving		% Daily Value
Vitamin K	2050 mcg	2563%
(as Vitamin K1-Phytonadione	1000 mcg;	
(Vitamin K2-Menaquinone-4	1000 mcg;	
(Vitamin K2-Menaquinone-7	50 mcg)	
Lecithin (from soy)	150 mg	*

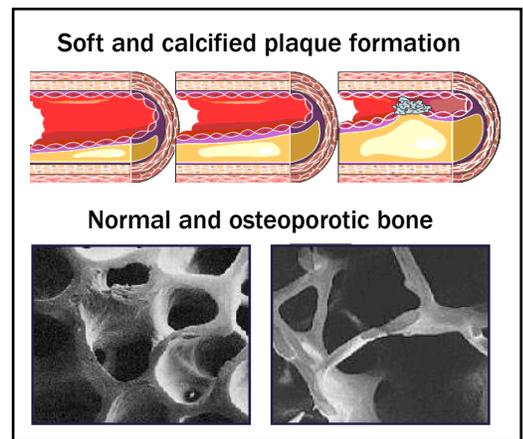
*Daily Value not established.

One capsule of Tri-K is a clinically useful dose, which can be used to correct subclinical vitamin K deficiency or at therapeutically higher levels to address specific conditions where vitamin K plays an important role.

Other Ingredients: Rice flour, magnesium stearate, silicon dioxide, microcrystalline cellulose.

Even though vitamin K1 and K2 (MK-4) are fat-soluble vitamins, their plasma half life is relatively short (around 2-8 hrs), and their effects on activating important proteins in the body may only be maximal for about 8-12 hours after supplementation [26]. Supplements that contain vitamin K, such as OsteoForce and Vitamin D Synergy, should be administered in divided doses, as evenly as possible throughout the day. Vitamin D Supreme and Tri-K, which contain K2 (MK-7), may be administered once a day because K2 (MK-7) has a very long plasma half-life.

Tri-K may be dosed at more than one capsule per day by health care practitioners, based on various clinical considerations. For example, some elderly patients that have severe osteoporosis or vascular calcification may benefit from 2 or more capsules of Tri-K per day. Anything above 2 caps per day may be considered well above a normal physiological dose, similar to the 15-45 mg dose of K2 (MK-4) used in Japanese studies [3], and should be used with caution. At this time, it is unclear what the optimal requirement for vitamin K is for pregnant and lactating women, but some studies have successfully used K1 at 10-20 mg pre-birth [81] and 5-20 mg during lactation [82, 83, 84] in order to prevent risk of hemorrhage in infants. If fat digestion is impaired, take vitamin K with DFH Phosphatidylcholine, Phosphatidylserine, LV-GB, Digestzymes or PaleoMeal (contains phosphatidylcholine).



Is it safe to take vitamin K at levels higher than AI (Adequate Intake)? Will it increase clotting?

The AI (Adequate Intake) for vitamin K (90-120 mcg) is sufficient for activating the liver enzymes involved in the carboxylation of the clotting proteins. When the body receives an amount of vitamin K that is well above the level needed for clotting protein activation (90-120 mcg), for example 1-3 mg, the liver secures the amount of vitamin K needed for carboxylating its clotting factors and the rest of the vitamin K is distributed to other tissues in the body. Once the liver clotting factors are maximized in function (by complete carboxylation), no amount of excess vitamin K can increase clotting performance any further. [10, 11, 23, 50]. Therefore, it is safe to say that clotting is not enhanced by vitamin K intakes above those necessary for optimal clotting function.

Drug Interactions

Anticoagulants designed as vitamin K antagonists (such as warfarin / Coumadin®) should not be taken with Tri-K or any products containing vitamin K. However, vitamin K does not interfere with the action of blood thinners such as heparin, antiplatelet agents (such as aspirin, Plavix, clopidrogel, abciximab, tirofiban, and eptifibatide), direct thrombin inhibitors (hirudin, argatroban), or thrombolytic agents (clot dissolving proteolytic enzymes) [96, 97, 98]. Anticoagulants that interfere with vitamin K were shown to cause osteoporosis or increase risk of fracture [78], increase arterial or heart valve calcification [17] and hypertension [86]. Some researchers recommend direct thrombin inhibitors as a safer substitute to these anticoagulants [79].

It is important to note that in addition to their anti-platelet effects, aspirin (acetyl-salicylic acid) and other salicylate-containing drugs, slightly inhibit vitamin K activation and recycling, thus creating an increased demand for vitamin K. The result is reduced thrombin formation (an effect similar to warfarin / Coumadin®) [90, 91, 94]. Vitamin K supplementation may overcome this effect, while not interfering with their antiplatelet (COX inhibition) action [93]. Aspirin was shown to increase bone loss and reduce fracture healing, which may be due to its effect on vitamin K metabolism, thus vitamin K supplementation may be warranted whenever aspirin or other salicylate-derived drugs are administered on a long-term basis [98,99]. Antibiotics may increase the need for vitamin K supplementation because: 1) They may kill gut bacteria that normally produce vitamin K. 2) They may interfere with vitamin K activation and recycling (similar to anticoagulants), 3) They may inhibit the activation of various proteins (carboxylation) by vitamin K. [90, 77]. Examples of such antibiotics are broad spectrum cephalosporins, such as cefamandol, moxalactam and cefoperazome. High dose vitamin E supplementation (above 1000 IU's) was shown to impair blood clotting by interfering with the vitamin K-dependent carboxylation reactions. [67].

Tests for Vitamin K status

Fasting plasma vitamin K1 levels are not a complete indicator of vitamin K status because they only reflect the previous day's intake. Vitamin K is metabolized at various rates depending on the form; K1 (6-12 hrs), K2 (MK-4) (2-4 hrs) or K2(MK-7) (3-6 days) . Vitamin K is easily metabolized throughout several days and it does not accumulate in the body [19, 26, 27, 28]. Plasma and urine % undercarboxylated osteocalcin is the best functional measure of vitamin K status, but is not yet commercially available.

For more information on vitamin K food sources, mechanisms of action, supplementation studies review and references, see "Vitamin K Addendum", found at www.DesignsForHealth.com, Product Tech Sheet section.

To contact Designs for Health, please call us at (800) 847-8302, or visit us on the web at www.designsforhealth.com.