K2 MK-7 & D3

TECHNICAL SUMMARY

Vitamins D_3 and K_2 have been extensively studied regarding their roles in calcium metabolism.* Research indicates that a synergistic relationship exists between vitamin K_2 and vitamin D_3, especially in terms of bone strength and cardiovascular health.* While vitamin D_3 is recognized for its role in calcium absorption and metabolism, it is vitamin K_2 that directs calcium to bones rather than joint spaces and arteries.* This product is formulated with a clinically relevant dose of MK-7, a unique, soy-free form of vitamin K_2 that has been shown to promote healthy vascular structures.*

Structure formula:

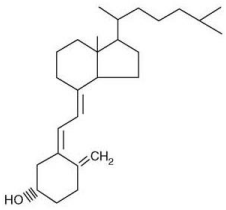

Figure 1: Vitamin D_3

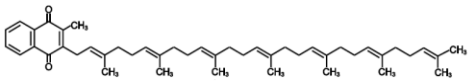

Figure 2: Vitamin K_2. 7 isoprenyl units attached to a 2-methyl1-1,4naphthoquinone structure

Chemical name:

Vitamin D_3: Cholecalciferol (activated 7-dehydrocholesterol; (3β,5*Z*,7*E*)-9,10-secocholesta-5,7,10(19)-trien-3-ol)

Vitamin K_2: 2-methyl-3-farnesylgeranylgeranyl-1,4-naphthoquinone (menaquinone-7; MK-7)

Allergen and Additive Disclosure: Not manufactured with wheat, gluten, soy, milk, egg, fish or shellfish ingredients. Cholecalciferol is from lanolin (sheep origin). MK-7 is produced using a soy-free substrate. Corn-derived ingredients are present in this product. Produced in a GMP facility that processes other ingredients containing these allergens.

Delivery Form: Vegetable capsules

ROLE AS NUTRIENT/FUNCTION

Vitamin K_2 is a generic term for a group of molecules of different sizes. This product has menaquinone-7 (figure 2), a purified form of vitamin K_2 with unique biological properties. Vitamin K is essential for the proper function (gamma-carboxylation of glutamyl amino acid residues) of GLA-proteins in the body, Including proteins involved in extracellular matrix mineralization such as osteocalcin in bones, and other matrix GLA-proteins (MGP) found in cartilage and artery walls.* Clinical data suggest, for example, that MK-7 supplementation is able to induce prolonged carboxylation of osteocalcin and MGP in the blood.*

Vitamin D_3's function in the body is well established allowing for the tight regulation of calcium levels in the blood, as well as phosphate homeostasis.* In addition, more recent discoveries have shown that vitamin D, as a hormone, is also involved in many other bodily functions such as regulation of cell proliferation, cell differentiation, immunomodulation, and cardiovascular health.*

Supplement Facts

Serving Size 1 Capsule

	Amount Per Serving	% Daily Value
Vitamin D (as D_3 Cholecalciferol) (from Lanolin)	125 mcg (5,000 IU)	625%
Vitamin K_2 (as Menaquinone-7) (MK-7) (MenaQ7®) (from chickpea)	180 mcg	†

† Daily Value not established.

Other ingredients: Microcrystalline Cellulose, Hypromellose (cellulose capsule) and Silicon Dioxide.

- **Vascular Health***
- **Structural Support***

SUGGESTED USAGE: Take 1 capsule daily with a meal, or as directed by your healthcare practitioner.

Preliminary data suggest that synergy exists between vitamin D_3 and vitamin K_2.* It appears that this synergy is the result of several combined biological functions, for example they are both involved in osteocalcin regulation in the body: vitamin D_3 regulates its production and vitamin K_2 is necessary for its activation.

NATUROKINETICS®

Liberation: K2 MK-7 & D3 vegetable capsules pass a standard disintegration test in water (<60 minutes).

Absorption: Both vitamin D_3 and K_2 are fat soluble vitamins. Following oral ingestion, MK-7 is rapidly and well absorbed in the intestine and enters blood circulation via the lymphatic system as part of the chylomicron fraction of plasma.

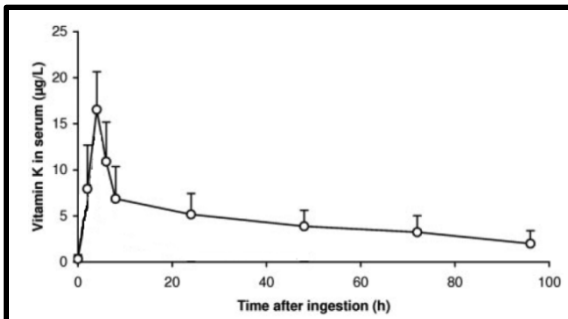

Figure 3: Circulating vitamin K concentrations following a single oral dose of 1 mg MK-7. Baseline level <0.05 mcg/L was subtracted from all values.

Like Vitamin K_2, Vitamin D_3 is absorbed with other dietary fats in the small intestine, enters the blood circulation via the lymphatic system and is transported in the chylomicron fraction of plasma.

Both Vitamin K_2 and D_3 are most efficiently absorbed when consumed with foods containing fat.

Distribution: MK-7 has a very long half-life. After oral ingestion it can be detected in the plasma for more than 48 hours and up to 92 hours.

MK-7's distribution in tissues has not been yet fully elucidated; however, it is known to be present in the liver, pancreas, heart and bone lipids.

Once vitamin D enters the circulation, it is cleared by the liver or stored in fat tissues within a few hours. However, the vitamin D deposited in fat is not readily available to exert its bodily functions.

Metabolism: In the bloodstream, chylomicrons carrying vitamin K are metabolized into chylomicron remnants which are cleared by the liver. MK-7 metabolism in the liver is only partially known, it is most likely degraded through omega- and beta-oxidation and the obtained metabolites are then conjugated with glucuronic acid.

Vitamin D is an inactive prohormone and must first be metabolized to its hormonal form before it can function. This metabolism is complex with a first phase occurring in the liver and a second phase in the kidney. It is tightly regulated by the parathyroid gland, which is sensitive to changes in blood calcium and phosphate levels.

Elimination: The products of MK-7 metabolism are excreted in the bile and urine.

The products of vitamin D metabolism are excreted through the bile into the feces, and very little is eliminated through the urine.

CLINICAL VALIDATION

- In a double-blind, randomized, placebo-controlled clinical study in a population of healthy post-menopausal women (n=244, 55-65 y.o.), supplementation with 180 mcg/d MK-7 for three years resulted in a significant improvement of vitamin K status and a decrease of age-related decline in bone mineral density and bone mineral content (BMC) (figure 4) as measured by bone densitometry (DXA).*
  In the same study, after three years of supplementation, women in the MK-7 group had a lower arterial stiffness as measured with carotid-femoral Pulse Wave Velocity (p=0.040 vs. placebo) and stiffness index (p=0.018 vs. placebo).*

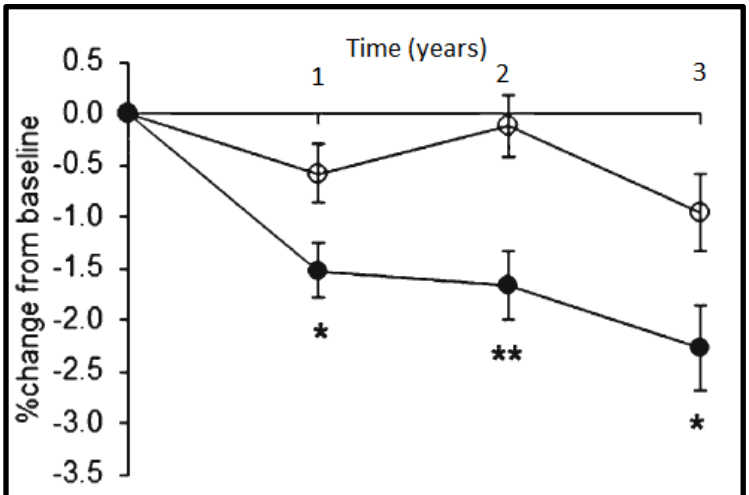

Figure 4: Evolution of bone mineral content in lumbar spine area overtime (3 years) with 180 mcg/d MK-7 (white circles) or placebo (black circles). *p<0.05 vs. placebo; **p<0.005 vs. placebo.

SAFETY INFORMATION

Tolerability: While vitamin D_3 is typically well tolerated, minor GI manifestations (nausea, abdominal discomfort) have been described with vitamin K_2 supplementation.

Contraindications: Individuals receiving vitamin K antagonists (VKA). Individuals with hypercalcemia.

INTERACTIONS

Drug Interactions: Possible interactions with cardiac glycosides, atorvastatin, thiazide diuretics, and anti-coagulant medication.

Supplement Interactions: Vitamin D increases calcium and magnesium absorption and may therefore interact with calcium and magnesium supplementation.

CoQ10 and vitamin K_2 have similar chemical structures, concomitant use may theoretically have an additive effect.

Interaction with Lab Tests: Theoretically, blood calcium and urinary calcium may be modified by a combined supplementation with vitamin K_2 and vitamin D_3. However this has not been clinically evaluated.

Osteocalcin blood levels can be increased by vitamin K_2 supplementation.

STORAGE

Store in cool, dry environment in a tightly sealed container. Store at ambient temperature. Protect from excessive heat, light and moisture.