Dietary Supplement Information for Physicians with Naturokinetics®

PRODUCT CODE: <u>P0379</u>
CATEGORY: MULTIVITAMINS

Liquid D3 & MK-7

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 D₃

Figure 2: Vitamin K₂. 7 isoprenyl units attached to a 2-methyl1-1,4naphthoquinone structure

Chemical Name:

Vitamin D_3 : Cholecalciferol (activated 7-dehydrocholesterol; $(3\beta,5Z,7E)$ -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 derived from chickpeas. Produced in a GMP facility that processes other ingredients containing these allergens.

Delivery Form: Liquid.

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 main 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 is also involved in many other bodily functions such as regulation of cell proliferation, cell differentiation, immunomodulation, and cardiovascular health.*

Supplement Facts

Serving Size 5 Drops (approx. 0.184 mL) Servings Per Container about 163

Amount Per Serving

% Daily Value

Vitamin D 62.5 mcg (2,500 IU) 313% (as D₃ Cholecalciferol) (from Lanolin)

Vitamin K₂ 100 mcg † (as Menaquinone-7) (MK-7) (MenaQ7[®]) (from chickpea)

† Daily Value not established.

Other ingredients: Medium-Chain Triglycerides (MCT Oil, Sunflower Oil, Safflower Oil, Soy-Free Vitamin E, Peppermint Oil and Rosemary Extract.

Bone and Cardiovascular Support*

SUGGESTED USAGE: Shake well. Take 5 drops daily, or as directed by your healthcare practitioner. Take directly or add to a beverage. Best when taken with a fat-containing meal.

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: Liquid D3 & MK-7 is already in a convenient easily absorbable liquid form.

Absorption: Both vitamin D₃ and K₂ are fat-soluble vitamins. Following oral ingestion, MK-7 is rapidly and well absorbed in the intestine and enters

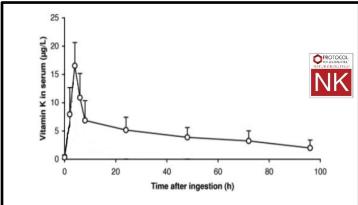


Figure 3: Circulating vitamin K concentrations following a single oral dose of 1 mg MK-7. Baseline level < 0.05 mce/L was subtracted from all values.



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blood circulation via the lymphatic system as part of the chylomicron fraction of plasma (Figure 3).

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

Distribution: 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, 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 (cholecalciferol) 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: MK-7 has a long half-life. After oral ingestion it can be detected in the plasma for more than 48 hours and up to 92 hours. 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 12-month, multi-group supplementation clinical study, 173 healthy post-menopausal women received dairy products enriched with Calcium (800 mg/d) & vitamin D (10 mcg/d) as well as either 100 mcg vitamin K₁ or 100 mcg MK-7. After 12 months of supplementation, authors observed a significant improvement of bone mass density in the lumbar spine and total body in the group receiving MK-7 compared to the control group (no supplementation) and baseline. (Figure 4)*

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.



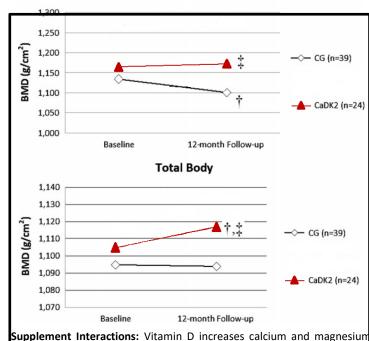


Figure 4: Changes in lumber spine and total-body bone mass density for women in the control group (CG) and the group receiving MK-7 (CaDK2). †p<0.05 compared to baseline value within group, ‡p<0.05 compared to control group. (Adapted from original publication presenting results for control group and MK-7 group only)

absorption and may therefore interact with calcium and magnesium supplementation.

Coenzyme Q10 is chemically similar to vitamin K_2 and can theoretically have vitamin K-like effects, including antagonism of warfarin. Concomitant use of coenzyme Q10 and vitamin K might cause additive effects and increase the risk of clotting in people taking anticoagulants.

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 K₂ supplementation.

STORAGE

Store in a cool, dry environment in sealed container. Store in ambient conditions (<80°F). Protect from excessive heat, moisture, air and light.