K2-D3 SAP

Science-based Vitamin K2-D3 combination for optimal health*

Vitamin K is involved in blood coagulation, bone metabolism and assists in reducing urinary calcium excretion.* Vitamin K is a cofactor in several biochemical pathways, especially, the γ-carboxylation of glutamyl residues in the bone protein osteocalcin, matrix γ-carboxyglutamyl protein, and protein S.* Vitamin K2 is the most potent form, exerting the highest gamma-carboxylation activity when compared to other vitamin K forms.* Vitamin D3 is a critical vitamin to overall human health.* Suboptimal levels of serum hydroxyvitamin D may contribute to a host of disease processes including cardiovascular disease, cancer, autoimmune diseases and infections.*

SUPPLEMENT FACTS

Serving Size: 4 drops **Servings:** Approx 131

	Amount Per Serving	% Daily Value
Vitamin D (1000 IU) (as cholecalciferol)	25 mcg	125%
Vitamin K (as MK-7)	120 mcg	100%

**Daily Value not established

Other ingredients: Medium- chain triglycerides.

Contains no: Gluten, soy, wheat, eggs, dairy, yeast, citrus, preservatives, artificial flavor or color, starch, or sugar.

This product is non-GMO and vegan friendly.

K2-D3 SAP contains 15 ml per bottle.

DIRECTIONS FOR USE

Adults: Shake well. Take 4 drops daily or as directed by your healthcare practitioner.
Store in a cool dry place.

INDICATIONS

K2-D3 SAP can help:

- Improve bone mineral density, support healthy bone development and alleviate osteoporosis.*
- Enhance cardiovascular health by reducing coronary calcification and mitigation of hypertension.*
- Support healthy immune function by stimulating the innate immune response.*
- Prevent development of several autoimmune diseases.*
- Support management of various types of cancer, including colon, breast and prostate cancers.*

Do not use if seal is broken. Keep out of reach of children.

CAUTIONS AND WARNINGS

Consult a healthcare practitioner prior to use if you are taking blood thinners.

PURITY, CLEANLINESS, AND STABILITY

All ingredients listed for each **K2-D3 SAP** lot number have been tested by an ISO 17025 accredited third-party laboratory for identity, potency, and purity.

*** These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.**

Scientific Advisory Panel (SAP): adding nutraceutical research to achieve optimum health

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VITAMIN K2 (MENAQUINONE-7)

Vitamin K is a fat-soluble vitamin that is involved in blood coagulation, is required for bone metabolism, and assists in reducing urinary calcium excretion.[1, 2] Vitamin K1 (phylloquinone) is present in green leafy vegetables and other plants, whereas vitamin K2 (menaquinone) is present in liver, meats, and foods prepared by fermentation, such as cheeses.[1, 2] Vitamin K is a cofactor in several biochemical pathways, especially, the γ-carboxylation of glutamyl residues in the bone protein osteocalcin, matrix γ-carboxyglutamyl protein, and protein S. Deficiency of each of these vitamin K-dependent proteins is associated with osteopenia.[1, 3] Studies have found that a high concentration of undercarboxylated osteocalcin and low dietary phylloquinone intake, resulting in low concentration of serum vitamin K, are associated with lower bone mineral density (BMD) and increased risk of hip fracture.[1, 2] Vitamin K2 is the most potent form, exerting the highest gamma-carboxylation activity when compared to other vitamin K forms.[4, 5] In a study with postmenopausal women, researchers demonstrated that MK-7 supplementation significantly increases serum MK-7 levels, whereas MK-4 had no effect on serum MK-4 levels, attesting to the higher bioavailability and efficacy of vitamin K2 as MK-7.[7]

The risk of vitamin K deficiency is higher in individuals with significant liver impairment, those who suffer from conditions of fat malabsorption or those taking vitamin K antagonist anticoagulant drugs.[7, 8]

CLINICAL INDICATIONS

Osteoporosis

MK-7 influences bone formation by improving the function of osteoblasts. Mk-7 has been shown to upregulate the SXR target gene CYP3A4 in osteoblasts and induce synthesis of osteoprotegerin and OC (an indicator of osteoblast function) in osteoblasts.[9] In addition, preclinical studies have shown that MK-7 downregulates NF-κB activation in osteoblasts and osteoclasts, independent of γ-carboxylation pathway.[9]

Several human trials have found vitamin K2 effective in the treatment of osteoporosis, especially, where the incidence of osteoporosis is high in postmenopausal women.[2, 5, 10] In one study, where the effect of low-dose MK-7 supplementation on bone health was measured, 244 healthy postmenopausal women received for 3 years placebo or MK-7 (180 µg MK-7/day) capsules. MK-7 supplementation was found to significantly improve vitamin K status and decrease age-related decline in BMD at the lumbar spine and femoral neck and decrease the loss in vertebral height of the lower thoracic region at the mid-site of the vertebrae.[11]

Cardiovascular Health

Cross sectional human studies suggest that dietary vitamin K2 might reduce the risk of cardiovascular disease by reducing coronary calcification. In one study with 564 postmenopausal women where dietary intake of vitamins K1 and K2 was determined using a food-frequency Questionnaire, it was observed that vitamin K2 intake alone was associated with the trend toward decreased coronary calcification.[12] In another study with 6,057 women, aged 49-70 years, who were free of cardiovascular diseases at baseline, mean vitamin K2 intake of 29.1± 12.8 µg/day was inversely associated with the risk of coronary heart disease.[13] A study in 4500 elderly patients also demonstrated an inverse relationship between vitamin K2 intake and aortic calcification, myocardial infarction and sudden cardiovascular death.[14]

Cancer

Various preclinical studies and case reports suggest the anticancer effects of vitamin K2 administration to positively inhibit cancer cells. Vitamin K2 due to its very limited toxicity can be a useful option for prevention of cancer and clinical therapy of cancer. However, more studies are warranted to investigate the effects of vitamin K2 as MK-7 in cancer therapy.[15]

VITAMIN D3

Vitamin D has 2 forms: vitamin D2, called ergocalciferol, and D3, cholecalciferol.

Since few foods have naturally high vitamin D content, the majority of dietary vitamin D is ingested through fortified foods or supplements.[1] Vitamins D3 undergoes metabolism in the liver and is converted to 25-ydroxyvitamin D and then hydroxylated in the kidney to the biologically active 1,25-dihydroxyvitamin D, which predominately acts in the duodenum and increases calcium absorption, as well as acts on bone cells to mobilize calcium stores.[16]

CLINICAL INDICATIONS

Bone Health

The function of vitamin D is to maintain serum calcium and phosphorus concentrations through regulating calcium absorption from the intestine or calcium reabsorption from bone, making vitamin D necessary for maintenance of healthy bone. The role of vitamin D insufficiency in osteoporosis is strongly recognized. For men and women over 50 years of age, evidence suggests that the plasma level of 25(OH)D needed to minimize fracture risk is ≥ 50 nmol/L, with 75 nmol/L being a more optimal level, and that an intake of 800–2000 IU/day of vitamin D3 is needed to bring the population average to this level.[17, 18]

Immune Function

A study in postmenopausal women either the common cold or influenza suggested lower occurrence of common cold or influenza in the treatment groups supplemented with 800 or 2000 IU of Vitamin D3 compared to the placebo group.[19] Vitamin D may contribute to the prevention and perhaps the treatment of both infections and autoimmune diseases. 1,25-Dihydroxyvitamin D [1,25(OH2)D] has both immunoregulatory and anti-inflammatory properties. Immune cells, including macrophages, dendritic cells and B cells, have the ability to respond to and synthesize 1,25(OH2) D, which results in the enhancement of innate immunity while simultaneously inhibiting the autoimmune response mediated by T helper cells (Th1).[20, 21]

Cancer

Vitamin D is known to promote cellular differentiation, arrest cell proliferation and decrease the growth of various tumours in laboratory animals.[16] A meta-analysis of case-controlled studies of patients with or without colon cancer demonstrated that for every 20 ng/ml increase in serum 25(OH)D levels, the chances of colon cancer were reduced by more than 40%.[16] Also, observational studies reported a lower risk of breast cancer among women with the highest 25(OH)D levels compared to the women with the lowest readings.[16] In an animal model study, vitamin D-deficient mice exhibited significantly accelerated bone turnover, with increased total tumour area and tumour mitotic activity compared to the control group.[22]

Cardiovascular Disease

A meta-analysis suggested that serum levels of 25(OH)D were inversely associated with hypertension.[23] Observational studies suggest that low 25(OH) D levels increase cardiovascular mortality.[16]

VITAMIN K2 AND D3 SYNERGY

Vitamins K2 and D3 have been suggested to work synergistically to improve calcium absorption. A preclinical study evaluated the effects of vitamin MK-7, alone or in association with vitamin D3 in differentiating human mesenchymal stem cells along the osteoblastic lineage. Combined administration of vitamin K2 as MK-7 with vitamin D3 profoundly influenced vascular endothelial growth factor and its receptor fms-related tyrosine kinase 1 (crucial factor in both angiogenic and osteogenic processes). These preclinical results underscore the synergistic effects of MK-7 and D3 co-supplementation in the bone-healing process. Moreover, at the protein level co-association of vitamins might provide an optimal balance between induction and carboxylation of osteocalcin, essential for its functionality in the extracellular matrix.[24]

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