Opti Active D & K2

Highly Bioavailable Vitamin D & K2

Available in **60 & 120 softgel capsules**

Opti Active D & K2 contains 10 micrograms of the active form of vitamin D, calcifediol monohydrate, for superior bioavailability, along with bioactive MK-7. The combination of calcifediol and K2 creates an optimal formula for bone health and strength, as well as supporting bone mineralisation.

Opti Active D & K2 plays a key role in the development and maintenance of healthy bones. Vitamin D helps calcium absorption, and a diet deficient in calcium can lead to osteoporosis in later life. This formula also helps support artery health and muscle function.

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- Opti Active D & K2 has been formulated to be included in therapeutic treatment plans to promote optimal endogenous levels of vitamin D and vitamin K2 in the body, while maximising patient compliance with 1 capsule per day dosage.
- Unique formula that combines clinically effective doses of calcifediol with vitamin K2 (menaquinone-7) (MenaQ7®) in a flaxseed oil base.
- Calcifediol has 3x per mcg superior bioavailability to colecalciferol.
- Vitamin K2 as menaquinone-7 has been found to be better utilised and more effective in supporting both bone and blood vessel heath than supplemental vitamin K1.

Active Ingredients

Each softgel capsule contains:

Calcifediol monohydrate	10 mcg
Menaquinione-7 (vitamin K2)(MenaQ7®)	180 mcg

Directions for use: Adults: 1 softgel per day or as directed by a health care practitioner.

Key Features & Benefits

Calcifediol

Calcifediol is a metabolically active form of vitamin D, which bypasses the need for metabolic conversion in the liver. It is a form of vitamin D that has superior bioavailability to the colecalciferol form. As the form of vitamin D that circulates in the blood, a lower amount of calcifediol is required to support the same therapeutic effects and activity in the body compared to higher dosages of colecalciferol.[1]

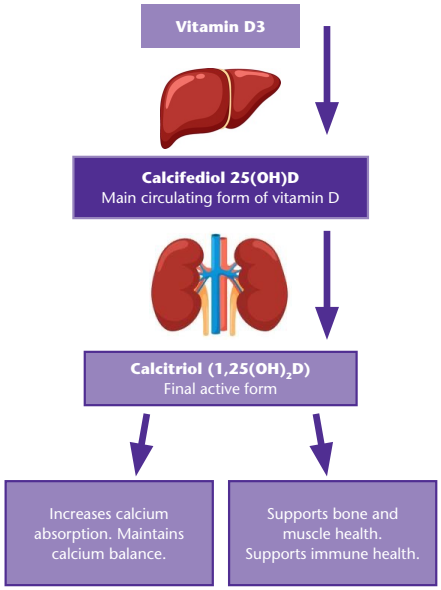
CLINICAL EVIDENCE

Bioavailability of Calcifediol

Calcifediol is hydrophilic, more soluble and has a higher rate of intestinal absorption (93%) compared to vitamin D3 as colecalciferol (79%), which is lipophilic and requires more complex absorption mechanisms.[1] Absorption of colecalciferol is reduced even further in people with intestinal fat malabsorption. Furthermore, calcifediol has a more linear and predictable dose-response relationship.[1]

Calcifediol is already in an active form, bypassing the need for enzymatic conversion in the liver, whereas colecalciferol is metabolically inactive. This is an especially important consideration in those with compromised liver health or who are taking medication that affects the hepatic CYP450 enzyme system.[1,2] This may also be an important consideration in people with obesity as colecalciferol is

Figure 1: Calcifediol is More Bioavailable and Bypasses Conversion in the Liver



more likely to be sequestered into adipose tissue due to its lipophilic properties. This may result in less vitamin D being available for conversion to calcifediol in the liver.[1]

In addition, calcifediol may be better utilised in those with a magnesium deficiency as magnesium is required for the enzymatic conversion of vitamin D3 to calcifediol in the liver.[2]

Vitamin D as calcifediol may therefore be more easily assimilated in those with decreased intestinal absorption capacity, liver or pancreatic insufficiency, obesity or magnesium deficiency.[1,2,4,5] Calcifediol has also been identified as the vitamin D of choice when raising vitamin D faster is important and for those with osteomalacia, non-dialysis kidney disease or men with hypogonadism.[1]

Calcifediol results in a more rapid increase in serum vitamin D compared to vitamin D3.[3] In a study comparing calcifediol (20 mcg/day) to colecalciferol (vitamin D3) (60 mcg / 2400 IU), 88% of participants with calcifediol reached sufficient vitamin D status in 4 weeks and mean sufficient levels were reached after 4 weeks.[4] In those taking colecalciferol, only 23% of participants reached sufficient vitamin D status after 4 weeks, while mean sufficient levels were not reached even after 16 weeks.[4]

The findings of 7 clinical trials show that daily doses of calcifediol were on average 3.2-fold more potent than vitamin D3 (relative to weight-dose basis).[3] Therefore, not only is calcifediol better absorbed and utilised than colecalciferol, and so corrects vitamin D deficiency promptly, but it can also be used at lower doses.[1]

Bone and Muscle Health

Studies have shown that vitamin D supplements, in combination with calcium may reduce postmenopausal bone loss, help maintain healthy bone mass, help prevent osteoporosis and help prevent osteoporosis-related falls and fractures. In fact, vitamin D deficiency has been recognised as an independent risk factor for falls and fractures.

Multiple clinical trials, reviews and meta-analyses have reported that supplemental intake of vitamin D, in combination with increased intake of calcium, may prevent hip or any type of fracture. Research also reports that vitamin D alone, may reduce the risk of falls among ambulatory or institutionalised older individuals with stable health by more than 20%.[6,7]

In addition, a 1-year double-blind, randomised controlled, multi-centre trial has shown calcifediol was faster and more effective in raising vitamin D to optimal levels than colecalciferol in a cohort of post-menopausal women (osteoporotic and non-osteoporotic).[8]

Vitamin D also helps maintain muscle strength, which may reduce the risk of falls and fractures. Deficiency may present as muscle pain and weakness, leg heaviness, increased body sway, rapid fatigue and difficulties getting up from a chair or climbing steps.[6-11]

A meta-analysis of 7 randomised-controlled trials (RCTs) reported that vitamin D as calcifediol has a significant positive effect on muscle strength parameters and that use may be beneficial in older people, not only for bone metabolism, but also to address muscle weakness.[12]

Vascular Health

Vitamin D deficiency has been associated with an increased risk of vascular dysfunction, arterial stiffening and cardiovascular disease.[13-16]

Vitamin D may support healthy vasculature via several mechanisms[13-16] including regulation of vascular function and vascular remodelling, influencing inflammatory mediators, promoting anti-atherogenic immune system cells and supporting blood pressure regulation (via renin-angiotensin system).[13-20]

Vascular calcification is a pathology characteristically observed in advanced age and is a feature of atherosclerosis. It has been observed that patients with severe atherosclerosis in coronary arteries have significantly lower serum calcifediol (25(OH)D) levels compared to patients without significant atherosclerotic lesions.[21,22]

Vitamin K2 (menaquinone-7)

Vitamin K is a fat-soluble vitamin that plays an important role in bone metabolism and bone turnover and supports vascular health and functions as a cofactor in the synthesis of blood coagulation factors.[20,21] There are two main forms of vitamin K, K1 and K2.[23]

Vitamin K2 is essential for calcium metabolism, bone metabolism and vascular health.[23-26] Main dietary sources of K2 include fermented foods such as dairy and soy products, with natto being especially rich in menoquinone-7, but not commonly part of a western diet. Vitamin K2 is also found in small amounts in meat, fish and eggs and some vitamin K2 is produced by gut bacteria. Vitamin K1, on the other hand, is involved primarily in the synthesis of blood coagulation factors in the liver. It is more readily available through dietary sources as it is found in dark leafy vegetables.[23,27]

Menaquinone-7 (MK-7) is a high-quality vitamin K2 that is the most efficiently absorbed and exhibits the greatest bioavailability of all the menaquinones.[28]

MECHANISM OF ACTION

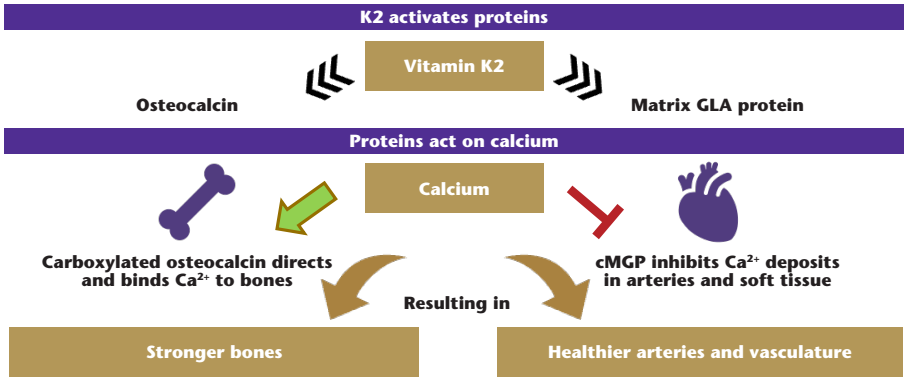
Bone Health

Vitamin K2 activates (stimulates carboxylation of) a protein known as osteocalcin, which is produced by bone osteoblasts.[27,29,30] Active osteocalcin then binds to calcium, leading to calcium being deposited into bones.[27,29,30,32] It also promotes bone mineralisation and alignment of apatite crystals and collagen fibres.[27, 29,30] Vitamin K2 as MK-7 has also been shown to have inhibitory effects on bone resorption and to regulate formation of osteoclasts (which break bone down).[29,30]

Vascular Health

Vitamin K2 inhibits abnormal soft tissue and blood vessel calcification and arterial stiffening.[24,25,27,29] It is essential for the activation, or carboxylation, of matrix GLA-protein (MGP) to cMGP, which inhibits calcium being deposited in blood vessels and so protects against vascular calcification.[25,27,30-33] In addition, vitamin K2 supports cardiovascular health through activation of osteocalcin, as well as another vitamin K-dependent protein Gas6, both of which play a secondary role in modulating the vascular calcification process via actions on vascular smooth muscle cells.[31]

Figure 2: Vitamin K2 is Important for Bone and Vascular Health



CLINICAL EVIDENCE

Bone Health

Higher vitamin K2 intake is related to a lower fracture incidence and improved bone density.[34] A meta-analysis of 19 RCTs, involving 6759 participants, found that vitamin K2 improves activation of osteocalcin, which facilitates calcium being moved into bone.[34] In addition, it was shown that vitamin K2 improves vertebral bone mineral density (BMD) and reduces the incidence of fractures in postmenopausal women.[34]

In a 3-year randomised controlled trial (RCT), vitamin K2 (as menaquinone-7) at a daily dose of 180 mcg has been shown to support bone health in postmenopausal women.[20] The results included significant reductions in aged-related loss of bone mass and BMD at the lumbar spine and femoral neck, improved bone strength and bone health and reduced loss of vertebral height. In addition, these benefits were sustained over the 3 years of the trial.[24]

Vascular Health

Studies demonstrate a strong association between vitamin K deficiency, arterial stiffness, vascular and valvular calcification, heart failure and cardiovascular mortality.[24]

Clinical trials have shown that higher intake of vitamin K2 has been associated with reduced coronary calcification and reduced risk of coronary heart disease (CHD).[24,31,32,35-37]

A 3-year randomised controlled trial reported that vitamin K2 (as menaquinone-7) at a daily dose of 180 mcg, improves arterial stiffness in healthy postmenopausal women, especially in women with high arterial stiffness.[37] Based on these findings, the effective recommended dose of vitamin K2 for vascular health is at least 180 mcg daily.[24]

In addition, epidemiological studies show that increased dietary intake of K2 (but not K1) is associated with a reduced risk of coronary heart disease. The Rotterdam study, a population-based study of almost 8,000 men and women over the age of 55, investigated factors that determined the occurrence of cardiovascular disease. All other factors being equal, participants with the highest vitamin K2 intake had a 50% lower risk of death from coronary heart disease and calcification of the coronary arteries than people with the lowest intake of vitamin K2.[36]

Combination of Vitamins D and K2

Multiple studies have demonstrated that vitamins D and K have a synergistic effects.[38]

Vitamin D as the active form (calcitriol), acts as a transcription activator for the synthesis of two vitamin K-dependent proteins, osteocalcin and matrix GLA protein (MGP).[38] Vitamin K2, in turn, is an essential co-factor for the carboxylation of these two proteins to their active forms.[38] Carboxylated osteocalcin results in increased bone mineral density.[38] Carboxylated MGP results in decreased vascular calcification.[38]

In summary, vitamin D is required for the intestinal absorption of minerals such as calcium, while vitamin K facilitates calcium being deposited into bones while preventing inappropriate calcification of the blood vessels. In addition, cells only produce osteocalcin and the matrix GLA protein (MGP) in the presence of vitamin D, while vitamin K is necessary to activate those proteins to carry out their functions.

CLINICAL EVIDENCE

Bone Health

Research reports that combined use of vitamin D and vitamin K2 appears to increase bone formation and bone mineral density, especially lumbar BMD, and may reduce the risk of vertebral fractures, in postmenopausal women with osteoporosis.[30,39-42]

The combination has been shown to have greater benefits in maintaining bone mass than use of either vitamin D or vitamin K2 alone, in early post-menopausal women with mild osteoporosis.[30,39-42]

Vascular Health

A synergistic effect of vitamins D and K to support cardiovascular health has been reported, with evidence suggesting the combination may reduce the risk of vascular calcification and atherosclerosis progression.[30,42,43]

The combination of poor vitamin K and vitamin D status has also been associated with an increase in blood pressure.[30,42,43]

Warnings

Calcifediol may have similar effects to Vitamin D. Consult your health care professional before taking in combination with other medicines. This medicine should not be taken in combination with supplements containing Vitamin D without medical advice.

Vitamins and minerals can only be of assistance if dietary intake is inadequate.

Use in children under 9 years is not recommended.

Precautions and Contraindications[23,44,45]

Vitamin D supplements should be used with caution in patients with hypercalcaemia, hyperparathyroidism, impaired renal function and sarcoidosis unless under medical supervision.

Vitamin K may antagonise and reverse the therapeutic anticoagulant effects of warfarin. The combination should be avoided, unless under medical supervision.

Adverse Effects[23,44,45]

Calcifediol and vitamin K are generally well-tolerated at normal therapeutic doses.

Pregnancy and Lactation[44]

Vitamin D and vitamin K are considered safe for use in pregnancy and lactation at normal therapeutic doses.

The RDI dose of vitamin D in pregnancy and lactation is 5 mcg daily (200 IU), with an upper level of intake defined as 80 mcg (3200 IU).

The AI dose of vitamin K in pregnancy and lactation is 60 mcg daily. There is no defined upper level of intake.

This product is indicated for use in adults. Use in children is not recommended.

**References available on request*

Bioclinic Naturals® Australia: Unit B, 10-16 South Street, Rydalmere, NSW, 2116 **1300 422 339**