



PRODUCT FACT SHEET

ULTRA K2-D3

Contains vitamin K2 (menaquinone 7 & 9) for calcium metabolism, bone health and cardiovascular health. Vitamin D3 (cholecalciferol) at 2000 IU per tablet. One to two tablets per day provides 2000-4000 IU of vitamin D, which is considered a physiological dose that maintains proper blood levels of 25(OH)D. Most blood work will suggest supplementation of at least 2,000 IU's per day.

BACKGROUND

- Vitamin D3 is required for absorption of calcium from the gut, regulation of serum calcium levels, and regulation of at least 1000 genes
- Vitamin K2, also known as menaquinone-4, menaquinone-7, menaquinone-9 and, are required for modification of proteins that deposit calcium in bones

ULTRA K2-D3

ITEM #: 3621-0060-01

DESCRIPTION

All natural cinnamon flavored, chewable tablet delivering both vitamins K2 and D3.

HOW SUPPLIED

60 tablets, cinnamon flavor.

DIRECTIONS

Take 1-2 tablets daily with or between meals or as directed by your doctor. Store in a cool place and keep from children.

Supplement Facts

Serving Size 1 Tablet Servings Per Container 60

Amount Per Serving	% Daily Value
Vitamin D3 (as cholecalciferol)	2000 IU 500%
Vitamin K2 (as mixed menaquinones)	80 mcg 100%

Other Ingredients: Sorbitol, fructose, rice bran, stearic acid, (vegetable source), cellulose, natural flavors, magnesium stearate (vegetable source), silicon dioxide.



ANABOLIC LABORATORIES

Pharmaceutical Made Nutritional Products Since 1924



PRODUCT:
ULTRA K2-D3

ITEM #: 3621-0060-01

BACKGROUND

In recent years, the importance of vitamin D has captured the attention of health care providers. We now know that vitamin D toxicity is exceedingly rare and that vitamin D is required for health expression in multiple body systems and not just for bone metabolism as previously thought. For example adequate vitamin D is needed for optimal function of the immune and cardiovascular system. And it appears that the average individual requires between 2,000-10,000 IU per day to maintain optimal serum levels of 25(OH)D^{1,2}. For more detail see the Anabolic Labs Fact Sheet for Clinical D 5000.

Research suggests that vitamin D and vitamin K2 each support bone and cardiovascular health, which makes a combination supplement an excellent choice. As with vitamin D, our knowledge of vitamin K has also grown in recent years, leading many to advocate the use of supplemental vitamin K2.

Phylloquinone is vitamin K1, which is found in green leafy vegetables, and its primary function is to activate prothrombin and other clotting factors. Coumadin "thins the blood" by antagonizing the action of vitamin K.

Menaquinone is vitamin K2 and there are multiple varieties, which are designated as MK-4 to MK-14. The most commonly discussed and supplemented variety is the short chain MK-4, which is found in meat. The longer chain menaquinones are attracting more attention as supplements and include MK-7, MK-8, MK-9, which are found in fermented foods such as cheese and curds. MK-7 is also found abundantly in a fermented soybean product called natto. While vitamin K2 influences coagulation proteins like K1, menaquinones uniquely influence calcium metabolism in relation to bone and cardiovascular health.

Unlike other nutrients, which often have multiple and often complicated functions, understanding vitamin K is straightforward because it has a single known major function. It is a cofactor for one enzyme, gamma-glutamylcarboxylase, which is located in the endoplasmic reticulum of certain tissues³. This enzyme functions to add a COOH group to the glutamic acid residue of certain proteins during protein synthesis via a process called posttranslational modification. In short, vitamin K is required by various cells to activate key proteins, such as prothrombin, osteocalcin, and vascular matrix Gla protein.

In the case of prothrombin and other clotting proteins, after being manufactured in hepatocyte ribosomes, they undergo posttranslational modification [or activation] in the endoplasmic reticulum by vitamin K-dependent gamma-

glutamylcarboxylase. The outcome is a properly functioning coagulation system that maintains appropriate hemostasis.

In osteoblasts, osteocalcin is first formed in ribosomes and then its glutamic acid residues undergo posttranslational modification [or activation] in the endoplasmic reticulum by vitamin K-dependent gamma-glutamylcarboxylase. The gamma-carboxylated glutamic acid in osteocalcin functions to bind calcium, such that when osteoblasts release carboxylated osteocalcin, it binds to hydroxyapatite in bone to increase bone mineral density (BMD)^{3,4}. In contrast, under-carboxylated osteocalcin, due to a lack of vitamin K2, does not bind as efficiently to calcium and is not as readily incorporated into the bony matrix. The blood level of under-carboxylated osteocalcin is thought to be a marker of BMD as it is correlated with hip bone mineral density and fracture risk in elderly women⁴.

In Japan, natto is consumed in large quantities and is a source of MK-7. Individuals consuming natto tend to have higher levels of carboxylated osteocalcin, better bone density and less osteoporosis⁵. While long-term studies have yet to be performed and demonstrate a preservation of bone density, supplementation with 360 mcg/day of MK-7 for one year in postmenopausal women⁴ and pre-pubertal girls⁶ has led to a reduction in circulating under-carboxylated osteocalcin, but not an increase in BMD. In patients with heart and lung transplants, a one-year double blind study with 180 mcg/day of MK-7 led to a favorable effect on bones mass. BMD increased more in heart than lung recipients, while bone mineral content increased only in lung recipients⁷. Longer-term studies are needed and it is possible that MK-7 exerts bone protective effects other than BMD.

In arterial walls, matrix gamma-carboxyglutamate (Gla) protein (MGP) is produced in vascular smooth muscle cells by the same ribosomal-endoplasmic reticulum posttranslational modification process. Vascular MGP is a strong inhibitor of vascular calcification⁸ and in contrast, significantly increased levels of under-carboxylated MGP have been identified in atherosclerotic vessels⁹. Vitamin K1 intake has not been correlated to coronary heart disease, while MK-7, MK-8, and MK-9 appear to be protective¹⁰. Research suggests that MK-7 is the preferred cofactor for the vascular gamma-glutamylcarboxylase enzyme and animal studies suggest that vitamin K2 supplementation can lead to a regression of arterial calcification¹¹. It is known that most subjects in the healthy population are not optimally protected against vascular calcification due to the presence of uncarboxylated MGP, suggesting that MK-7 supplementation may be an effective interventional strategy¹¹.



PRODUCT:
ULTRA K2-D3

ITEM #: 3621-0060-01

BACKGROUND

Supplemental MK-7 has a very long half-life and results in much more stable levels when compared to vitamin K1. MK-7 induces a more complete carboxylation of osteocalcin¹², and presumably vascular MGP and clotting factors.

Recent studies suggest that dietary-derived longer chain menaquinones may be protective against cancer expression^{13,14}, and it appears not to be related to gamma-carboxylation.

A considered mechanism is an inhibitory effect on proto-oncogenes, which fosters cell cycle arrest and apoptosis¹³.

Patients on anticoagulant therapy should not take MK-7 or other K2 varieties without supervision and monitoring by their attending physician. Researchers suggest that 50 mcg is safe upper limit of MK-7 and other longer menaquinones (MK-8, MK-9) for properly monitored patients taking anti-coagulants¹².

REFERENCES

1. Cannell JJ, Hollis BW. Use of vitamin D in clinical practice. *Alt Med Rev*. 2008; 13(1):6-20.
2. Hathcock JN, Shao A, Vieth R, Heaney R. Risk assessment for vitamin D. *Am J Clin Nutr* 2007; 85(1):6-18.
3. McCann JC, Ames BN. Vitamin K, an example of triage theory: is micronutrient inadequacy linked to diseases of aging? *Am J Clin Nutr* 2009;90:889-907.
4. Emaus N, Gjesdal CG, Almas B et al. Vitamin K2 supplementation does not influence bone loss in early menopausal women: a randomised double-blind placebo-controlled trial. *Osteoporos Int*. 2009 Nov 25. [Epub ahead of print].
5. Ikeda Y, Iki M, Morita A et al. Intake of fermented soybeans, natto, is associated with reduced bone loss in postmenopausal women: Japanese Population-Based Osteoporosis (JPOS) Study. *J Nutr*. 2006; 136:1323-28.
6. van Summeren MJ, Braam LA, Liliën MR et al. The effect of menaquinone-7 (vitamin K2) supplementation on osteocalcin carboxylation in healthy prepubertal children. *Brit J Nutr*. 2009; 102(8):1171-78.
7. Forli L, Bollerslev J, Simonsen S, et al. Dietary vitamin K2 supplement improves bone status after lung and heart transplantation. *Transplantation*. 2010;89:458-64.
8. Cranenburg EC, Vermeer C, Koos R et al. The circulating inactive form of matrix Gla protein (ucMGP) as a biomarker for cardiovascular calcification. *J Vasc Res*. 2008;45:427-36.
9. Schurgers LJ, Teunissen KJ, Knapen MH et al. Novel conformation-specific antibodies against matrix gamma-carboxyglutamic acid (Gla) protein: undercarboxylated matrix Gla protein as marker for vascular calcification. *Atheroscler Thromb Vasc Biol*. 2005; 25(8):1629-33.
10. Gast GC, de Roos NM, Sluijs I et al. A high menaquinone intake reduces incidence of coronary heart disease in women. *Nutr Metab Cardiovasc Dis*. 2009;19:504-10.
11. Schurgers LJ, Cranenburg EC, Vermeer C. Matrix Gla-protein: the calcification inhibitor in need of vitamin K. *Thromb Haemost*. 2008; 100:593-603.
12. Schurgers LJ, Teunissen KJ, Hamulyak K et al. Vitamin K-containing dietary supplements: comparison of synthetic vitamin K1 and natto-derived menaquinone-7. *Blood*. 2007; 109(8):3279-83.
13. Nimptsch K, Rohrmann S, Kaaks R, Linseisen J. Dietary vitamin K intake in relation to cancer incidence and mortality: results from the Heidelberg cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC-Heidelberg). *Am J Clin Nutr*. 2010; Mar 24 [Epub ahead of print as doi: 10.3945/ajcn.2009.28691]
14. Nimptsch K, Rohrmann S, Nieters A, Linseisen J. Serum undercarboxylated osteocalcin as a biomarker of vitamin K intake and prostate cancer risk: a nested case-controlled study in the Heidelberg cohort of the European Prospective Investigation into Cancer and nutrition. *Cancer Epidemiol Biomarkers Prev*. 2009;18:49-56.

THE ANABOLIC DIFFERENCE

Anabolic Laboratories' nutritional products are made in a registered, licensed and inspected pharmaceutical facility. Our in-house laboratories and manufacturing facilities are routinely inspected by the United States Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA). We also maintain a Good Manufacturing Practice (GMP) certification from the Natural Products Association.

As a pharmaceutical manufacturer, the standards used for raw materials, production and finished product testing exceed FDA requirements for the nutritional products industry. Our pharmaceutical requirements for manufacturing are the foundation for the guaranteed quality of our nutritional products. Anabolic Laboratories sets the nutritional supplement industry standard for label accuracy, potency and purity as dictated by the FDA for pharmaceutical and nutritional products.

