

## APPLICATIONS

- Immune System Support
- Cardiovascular Support
- Bone Health Support
- Neurological Support
- Vitamin Support



## INTRODUCTION

Vitamin D is a fat-soluble vitamin that may be synthesized in the body through a multi-step process. UVB rays convert 7-dehydro-cholesterol in the skin to pre-vitamin D<sub>3</sub>, which is converted to D<sub>3</sub> (cholecalciferol). Cholecalciferol is hydroxylated to calcidiol (25(OH)D) in the liver, and then to calcitriol (1,25(OH)<sub>2</sub>D) in the kidneys, at which time it is biologically active! The amount of vitamin D produced depends on several factors including latitude, season, skin exposure, skin color, and liver and kidney health.<sup>2</sup>

While outright vitamin D deficiency is rare, low vitamin D status may affect up to 75% of U.S. adults.<sup>3</sup> In supplement form, vitamin D is available as cholecalciferol (D<sub>3</sub>) or ergocalciferol (D<sub>2</sub>). D<sub>3</sub> is more effective than D<sub>2</sub> at maintaining vitamin D levels already within the normal range.<sup>4</sup> The DRI for Vitamin D is 15 mcg/day (600 IU) for ages 1-70 and 20 mcg/day (800 IU) for ages 70 and older,<sup>2</sup> as the ability to synthesize vitamin D declines with age.<sup>2</sup> Significant dietary sources of vitamin D include rainbow trout, sockeye salmon, eggs, and beef liver. Foods such as cow's milk and alternative plant milks are often fortified with vitamin D. Mushrooms, when treated with UV light, are a vegetarian source of vitamin D.<sup>5</sup>

Vitamin K is a fat-soluble vitamin that can be synthesized by colonic bacteria in the form of menaquinones (K<sub>2</sub>). Vitamin K encompasses a group of compounds with the chemical structure 2-methyl-1,4-naphthoquinone.<sup>6</sup> Deficiency is rare in adults, and when present, is usually from malabsorption, as occurs in celiac disease, in ulcerative colitis, or from bariatric surgery.<sup>7,8</sup> The adult DRI for Vitamin K is 90 mcg/day in women and 120 mcg/day in men.<sup>9</sup>

Food sources of vitamin K<sub>1</sub> include leafy green vegetables and soybeans, while food sources of vitamin K<sub>2</sub> include dairy, fermented foods and animal foods.<sup>5,8</sup> As a dietary supplement, Vitamin K is available as K<sub>1</sub> or K<sub>2</sub>, the latter of which is preferred due to better absorption and bioavailability.<sup>9,10</sup> Of the K<sub>2</sub> menaquinones, MK-4 and MK-7 are the most commonly available. While both are well-absorbed, the

MK-7 form is preferred due to a longer half-life.<sup>7,12</sup>

Together, D<sub>3</sub> and K<sub>2</sub> have synergistic roles in both bone and cardiovascular health.\* Vitamin D supports the production of vitamin-K-dependent proteins such as osteocalcin and matrix Gla protein, while vitamin K allows for their carboxylation and function.<sup>13,14</sup> Studies suggest that their concurrent use may be more effective than either alone.<sup>13</sup>

## IMMUNE SYSTEM SUPPORT

Vitamin D receptors and 1-alpha hydroxylase, the enzyme that converts calcidiol to active calcitriol, are found on a variety of immune cells.<sup>15,16</sup> In innate immunity, vitamin D helps support healthy monocyte function; in adaptive immunity, vitamin D may help to support immune tolerance and homeostasis.<sup>16,17,18</sup> Vitamin D may help maintain cytokines already within the normal range, and may additionally help to maintain dendritic cell function and T cell function already within the normal range.<sup>19</sup> Vitamin D 5000 IU may help with immune support, particularly during the winter season.<sup>20</sup> Other amounts have also been protective.<sup>21</sup>

## CARDIOVASCULAR SUPPORT

Vitamin D levels are associated with cardiovascular health.<sup>22</sup> Vitamin D may help to support heart health by maintaining insulin sensitivity, blood glucose, and blood lipids already within the normal range.<sup>23</sup> It may also help with homeostatic support of the renin-angiotensin-aldosterone system (RAAS).<sup>24</sup> Vitamin K is needed for the gamma-carboxylation of matrix Gla protein, which is important for vascular health.<sup>25</sup>

## BONE HEALTH SUPPORT

Vitamin D helps with bone support by facilitating the absorption of dietary calcium and regulating calcium and phosphorus.<sup>26</sup> Vitamin D also helps to maintain PTH already within the normal range, maintaining the calcium in bones and supporting normal bone density.<sup>27</sup> Vitamin K is needed for the gamma-carboxylation of osteocalcin, which is important for normal bone mineralization.<sup>28,29,30</sup> Vitamin D<sub>3</sub> at 5,000 IU per day may help to maintain normal z scores (p<0.001) and may help with postmenopausal bone support.<sup>31</sup>

Vitamin K<sub>2</sub>, both alone and with D<sub>3</sub>, helps to support bone health in early postmenopausal women (p<0.005), as evidenced by the maintenance of serum undercarboxylated osteocalcin (ucOC) already within the normal range.<sup>32</sup> Vitamins K<sub>2</sub> and D<sub>3</sub> together may help to maintain intact osteocalcin (OC) and bone alkaline phosphatase (BAP), serum markers of bone formation, already within the normal range (p<0.05), though K<sub>2</sub> alone did not show these benefits.<sup>32</sup>

## OTHER USES

### Neurological Support

Vitamin D receptors have been found in neurons and glial cells, and vitamin D may help with neurological support.<sup>33,34</sup> Vitamin D has many roles in the nervous system, including the regulation of neurotransmitter synthesis.<sup>33</sup> It may help microglia to maintain levels of cytokines, IL-6, IL-12, and TNF-alpha already within the normal range.<sup>35</sup> Vitamin D may support healthy cognition and help to maintain A-beta-related biomarkers already within the normal range.<sup>36</sup> Vitamin K may help to support healthy proliferation, differentiation, and lifespan of brain cells through its role in sphingolipid metabolism, which may help to support healthy cognition.<sup>37</sup>

### Vitamin Support

This product includes 125 mcg (5000 IU) of vitamin D<sub>3</sub> as cholecalciferol, which is 625% of the Dietary Reference Intake (DRI). This product also includes 150 mcg of vitamin K<sub>2</sub> as Menaquinone-7, which is 125% of the DRI.<sup>2,9</sup>

## SAFETY AND CAUTIONS

Vitamin D is generally well tolerated. Numerous studies have used a dose of 5,000 IU/day safely and without adverse effects.<sup>38,39</sup> Long-term, high-dose vitamin D may result in hypercalcemia, azotemia, or anemia.<sup>40</sup> Possible side effects of vitamin D toxicity include hypertension,<sup>40</sup> pancreatitis,<sup>40</sup> elevated INR,<sup>41</sup> osteoporosis,<sup>40</sup> or

kidney stones.<sup>42</sup> Vitamin D may increase the absorption and toxicity of aluminum in patients with kidney failure.<sup>43</sup> Vitamin D may induce CYP3A4 enzymes, which may decrease absorption of CYP3A4 substrates such as atorvastatin.<sup>40</sup> Taken concurrently with thiazide diuretics, Vitamin D may increase the risk for hypercalcemia,<sup>44</sup> which may decrease the effectiveness of anti-arrhythmics.<sup>45</sup>

Vitamin K is generally well tolerated. Side effects may include nausea, stomach upset, and diarrhea.<sup>46</sup> This supplement should not be taken with warfarin, as Vitamin K antagonizes the anticoagulant effects.<sup>47</sup>

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

**\* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.**

**NutraMedix**

**VITAMINS D<sub>3</sub> & K<sub>2</sub>**

SUPPORTS IMMUNE, CARDIOVASCULAR, AND BONE HEALTH<sup>†</sup>

Dietary Supplement  
90 Vegetable Capsules

**Supplement Facts**  
Serving Size 1 Capsule  
Servings Per Container 90

Amount Per Serving	% Daily Value
Vitamin D3 (as Cholecalciferol)	125mcg (5000 IU) 625%
Vitamin K2 (as Menaquinone-7)	150mcg 125%

**Other Ingredients:** Microcrystalline Cellulose, Vegetable Capsule, Dicalcium Phosphate, Vegetable Magnesium Stearate

**NutraMedix**  
Jupiter, Florida 33458 USA  
www.nutramedix.com  
561-745-2917

KEEP OUT OF REACH OF CHILDREN  
STORAGE: Keep tightly closed in a dry place at room temperature. (59-86°F or 15-30°C)  
SUGGESTED USE: Take one capsule daily after a meal or as directed by your physician. Do not use if pregnant or nursing. Stop use if adverse reactions develop.  
Do not use if taking Coumadin (warfarin).

†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.

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DIETARY SUPPLEMENT  
GLUTEN FREE  
VEGETARIAN FRIENDLY

1000000

## REFERENCES

- Bikle, D. D. (2014). *Chemistry & Biology*, 21(3), 319–329.
- Institute of Medicine. (2011). *Dietary Reference Intakes for calcium and vitamin D*. Washington, DC: The National Academies Press.
- Binkley, N., Ramamurthy, R., & Krueger, D. (2010). *Endocrinology and Metabolism Clinics of North America*, 39(2), 287–contents.
- Martineau, A. R., Thummel, K. E., et al. (2019). *The Journal of Clinical Endocrinology and Metabolism*, 104(12), 5831–5839.
- Office of Dietary Supplements. (2021). Office of Dietary Supplements - Vitamin D. Ods.od.nih.gov. Retrieved 18 August 2021, from <https://ods.od.nih.gov/factsheets/VitaminD-HealthProfessional/>.
- Booth S. L. (2012). *Food & Nutrition Research*, 56, 103402/fnr.v56i0.5505.
- Office of Dietary Supplements. (2021). Office of Dietary Supplements - Vitamin K. Ods.od.nih.gov. Retrieved 18 August 2021, from <https://ods.od.nih.gov/factsheets/vitaminK-HealthProfessional/>.
- Sherf-Dagan, S., Goldenshluger, A., et al. (2019). *Surgery for Obesity and Related Diseases*, 15(8), 1402–1413.
- Institute of Medicine. (2001). Panel on Micronutrients. *Dietary Reference Intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc*. Washington (DC): National Academies Press (US). Available from: <https://www.ncbi.nlm.nih.gov/books/NBK222310/>
- Shearer, M. J., Bach, A., & Kohlmeier, M. (1996). *The Journal of Nutrition*, 126(4 Suppl), 118S–6S.
- Halder, M., Petsophonsakul, P., et al. (2019). *International Journal of Molecular Sciences*, 20(4), 896.
- Schurgers, L. J., Teunissen, K. J., et al. (2007). *Blood*, 109(8), 3279–3283.
- van Ballegooijen, A. J., Pilz, S., et al. (2017). *International Journal of Endocrinology*, 2017, 7454376.
- Kidd P. M. (2010). *Alternative Medicine Review: A journal of clinical therapeutic*, 15(3), 199–222.
- Priett, B., Treiber, G., et al. (2013). *Nutrients*, 5(7), 2502–2521.
- Siddiqui, M., Manansala, J. S., et al. (2020). *Nutrients*, 12(9), 2879.
- Szymczak, I., & Pawliczak, R. (2016). *Scandinavian Journal of Immunology*, 83(2), 83–91.
- Mpandzou, G., Ait Ben Haddou, E., et al. (2016). *Revue Neurologique*, 172(2), 109–122.
- Iijima, H., Shinzaki, S., & Takehara, T. (2012). *Current Opinion in Clinical Nutrition and Metabolic Care*, 15(6), 635–640.
- Jung, H. C., Seo, M. W., et al. (2018). *International Journal of Environmental Research and Public Health*, 15(9), 2003.
- Martineau, A. R., Jolliffe, D. A., et al. (2017). *BMJ (Clinical research ed.)*, 356, i6583.
- Judd, S. E., & Tangpricha, V. (2009). *The American Journal of the Medical Sciences*, 338(1), 40–44.
- Podzolkov, V. I., Pokrovskaya, A. E., & Panasenko, O. I. (2018). *Terapevticheskiy Arkhiv*, 90(9), 144–150.
- Giménez, V., Sanz, R. L., et al. (2020). *Current Protein & Peptide Science*, 21(10), 948–954.
- El Asmar, M. S., Naoum, J. J., & Arbid, E. J. (2014). *Oman Medical Journal*, 29(3), 172–177.
- Charoenngam, N., & Holick, M. F. (2020). *Nutrients*, 12(7), 2097.
- Khundmiri, S. J., Murray, R. D., & Lederer, E. (2016). *Comprehensive Physiology*, 6(2), 561–601.
- Kodama, Y., Okamoto, Y., et al. (2017). *Brain & Development*, 39(10), 846–850.
- Zoch, M. L., Clemens, T. L., & Riddle, R. C. (2016). *Bone*, 82, 42–49.
- Wen, L., Chen, J., et al. (2018). *Molecular Medicine Reports*, 18(1), 3–15.
- Mocanu, V., Stitt, P. A., et al. (2009). *The American Journal of Clinical Nutrition*, 89(4), 1132–1137.
- Yasui, T., Miyatani, Y., et al. (2006). *Gynecological Endocrinology: The official journal of the International Society of Gynecological Endocrinology*, 22(8), 455–459.
- Moretti, R., Morelli, M. E., & Caruso, P. (2018). *International Journal of Molecular Sciences*, 19(8), 2245.
- Di Somma, C., Scarano, E., et al. (2017). *International Journal of Molecular Sciences*, 18(11), 2482.
- Boontanrart, M., Hall, S. D., et al. (2016). *Journal of Neuroimmunology*, 292(2016), 126–136.
- Jia, J., Hu, J., et al. (2019). *Journal of Neurology, Neurosurgery, and Psychiatry*, 90(12), 1347–1352.
- Alisi, L., Cao, R., et al. (2019). *Frontiers in Neurology*, 10, 239.
- Bhargava, P., Fitzgerald, K. C., et al. (2017). *JCI insight*, 2(19), e95302.
- Han, Q., Li, X., et al. (2019). *Journal of the International Society of Sports Nutrition*, 16(1), 55.
- Natural Medicines. (2022, January 31). Vitamin D [monograph]. <http://naturalmedicines.therapeuticresearch.com>
- Carlton, S., Clopton, D., & Cappuzzo, K. A. (2010). *The Consultant Pharmacist: The journal of the American Society of Consultant Pharmacists*, 25(3), 171–177.
- Letavernier, E., & Daudon, M. (2018). *Nutrients*, 10(3), 366.
- Demontis, R., Leflon, A., et al. (1986). *Clinical Nephrology*, 26(3), 146–149.
- Jones, G. (2008). *The American Journal of Clinical Nutrition*, 88(2), 582S–586S.
- Bar-Or, D., & Gasiel, Y. (1981). *British Medical Journal (Clinical research ed.)*, 282(6276), 1585–1586.
- Natural Medicines. (2021, August 19). Vitamin K [monograph]. <http://naturalmedicines.therapeuticresearch.com>
- Crowther, M. A., Ageno, W., et al. (2009). *Annals of Internal Medicine*, 150(5), 293–300.