

# Vitamin D Supreme

5,000 IU vitamin D per serving with vitamin K1 and K2



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Vitamin D Supreme provides a clinically useful dose of vitamin D3, providing 125 mcg (5000 IU) per one capsule serving, along with 550 mcg vitamin K in both K1 and the MK-7 form of K2, which has superior bioavailability. Both of these forms of vitamin K are important to health: vitamin K1 (the naturally-occurring form of vitamin K in vegetables) and vitamin K2 as MK-7, which is a product of fermentation and has the special property of metabolizing slowly throughout the day. Vitamins D and K are essential for optimal bone and arterial health and for maintaining the immune system in proper balance. The amount of vitamin D and K in this formula may help correct the deficiencies of a majority of patients that do not get adequate sun exposure and/or dietary sources of these vitamins and may be a necessary dose where more aggressive repletion is required.\*

## Rationale for inclusion of vitamin K

Vitamin K is vital for directing the transport of calcium into bone and teeth for optimal strength. Increasing the amount of vitamin D, via supplementation, in the presence of inadequate levels of vitamin K, can increase the risk of calcium deposition in arteries and soft tissue and have a very negative effect on artery elasticity. This is due to vitamins D and K's interaction in the use of Matrix Gla Protein (MGP), which is a strong inhibitor of arterial calcification. The expression of MGP is vitamin D dependent and the gamma-carboxylation step, making it active, is vitamin K dependent.

Osteocalcin is the most well-known Gla protein. It has been widely recognized for its importance in bone density and requires vitamin K to work properly. Vitamin K is necessary for the carboxylation (the addition of a carboxyl group) of osteocalcin. Undercarboxylated osteocalcin cannot regulate calcium, and thus, increases the risk of calcium being deposited in arteries and soft tissue, thus increasing the risk of atherosclerosis.

Although it is classified as a vitamin, vitamin D more closely resembles and functions like a steroid hormone that contributes in multiple ways to the optimal function of human physiology.<sup>1</sup> Vitamin D receptors (VDR) are found throughout the body and have been shown to influence the expression of thousands of genes that result in explicit physiological actions by 1,25 dihydroxyvitamin D.<sup>3</sup> This fat-soluble vitamin is widely recognized for its critical role in maintaining optimal bone and arterial health, and for supporting proper immune function; however, its function far surpasses this, with many facets likely yet to be identified and elucidated. For example, vitamin D helps regulate phosphorus balance,<sup>2</sup> is needed for cell differentiation,<sup>2</sup> may improve insulin sensitivity and glucose metabolism,<sup>4,5</sup> and is associated with decreased risk of cancer mortality.<sup>4,6,7</sup>

Vitamin D plays a role in brain development in early life as well as brain function in adults, which may explain in part the associations between vitamin D deficiency, depressed moods,<sup>8</sup> seasonal disorders, cerebrovascular diseases,<sup>9</sup> impaired cognition,<sup>10</sup> and other neurological disorders such as multiple sclerosis,<sup>4</sup> and the improvements some patients report in these symptoms upon supplementation. In a study that looked at 290 patients with mental illness, 272 (94%) showed clinical vitamin D inadequacy or deficiency (VDID), indicating that deficiency is greater in patients with mental illness than in the general population.<sup>11</sup> In animals, chronic vitamin D deficiency increases the risk of developing chronic neurodegenerative diseases; chronic degenerative neurological diseases in humans are linked with vitamin D deficiency.<sup>4</sup> Furthermore, vitamin D elicits vasoprotective effects via mediating the activity of eNOS, and suppressing NF- $\kappa$ B signaling and proinflammatory cytokine production; vitamin D deficiency is a risk factor for endothelial dysfunction.<sup>12</sup>

Vitamin D3 (cholecalciferol) is synthesized in the skin from cholesterol in response to absorbing UVB rays. It then gets converted in the liver to 25-hydroxycholecalciferol, known as 25(OH)D3, which is the best biomarker for vitamin D status as it is the most stable and abundant vitamin D metabolite in human serum. It finally gets converted into its hormonally active form 1,25 dihydroxycholecalciferol—1,25 (OH)D3—in the kidneys.<sup>1</sup> Serum vitamin D concentrations between 50 and 125 nmol/L appear to be sufficient and safe.<sup>4</sup> However, vitamin D levels below 30 nmol/L is considered the threshold for hypovitaminosis D and associated with increased risk of rickets/osteomalacia,<sup>4</sup> and has become a major global public health concern, with epidemiological findings showing nearly one billion people worldwide to be deficient, while 50% of the population present with vitamin D insufficiency.<sup>13</sup>

## Benefits\*:

- Supports bone and hard tissue health<sup>1,2,4</sup>
- Helps reduce the risk of osteoporosis/osteomalacia<sup>2,4,14,15</sup>
- Supports arterial health<sup>2,12</sup>
- Helps reduce the risk of atherosclerosis<sup>2</sup>
- Helps regulate gene expression and cellular differentiation<sup>2,3</sup>
- Helps regulate phosphorus balance in the body<sup>2</sup>
- Supports neurological function, brain development, and enhance mood<sup>8</sup>
- Helps maintain healthy immune system balance and inflammatory response<sup>2,17-21</sup>
- May improve vaginal health of menopausal women<sup>25</sup>

Available in 30, 60, & 180 count

Many patients will require a higher dose of vitamin D in order to achieve optimal vitamin D status. According to the 2nd International Conference on Controversies in Vitamin D, 4,000 - 10,000 IU/day is considered a safe range for health care practitioners to use in the short term that will not result in serum levels above 250 nmol/L.<sup>4</sup>

### Vitamin D and Bone Health

Vitamin D assists with proper bone and tooth health and is important for cellular metabolism, as it controls calcium homeostasis. Vitamin D facilitates intestinal calcium absorption and reduces calcium excretion by the kidneys, providing calcium necessary for bone mineralization. Vitamin D is vital for normal growth and development in children and adolescents with peak bone mass occurring in the late teenage years, increasing about 40 times from birth to adulthood.<sup>14</sup> The risk of osteoporosis has its roots in childhood and adolescence, as the rate of cortical bone remodeling is as high as 50% per year in young children.<sup>14</sup> It is clear in research that vitamin D is critical in the prevention of rickets and osteomalacia, and that supplementation may prevent or help with sarcopenia in elderly populations.<sup>4,15</sup> A meta-analysis reported that in people over age 60, high serum 25(OH)D concentrations (with adequate calcium intake) reduce the risk of hip fractures compared to low vitamin D levels.<sup>4,16</sup>

### Vitamin D and Immune Health

Vitamin D is essential for the immune system, as it modulates the response of the innate and adaptive immune system via VDR. VDR is the critical transcription factor in differentiating lymphocytes within the bone marrow into monocytes and granulocytes.<sup>17</sup> Via toll-like receptors and macrophages, vitamin D stimulates the recognition of bacterial pathogens in monocytes and inhibits *M. tuberculosis* proliferation.<sup>17</sup> Vitamin D is able to regulate Th1 and Th2 lymphocyte balance and downregulate the expression of inflammatory cytokines overall. 1,25(OH)D<sub>3</sub> has been shown to heavily influence and shift dendritic cells' and macrophages' intracellular metabolism, metabolically reprogramming their role in inflammation and autoimmunity by altering these cells' phenotypic expression.<sup>18</sup> In fact, research shows that priming of naive CD4+ T cells with vitamin D-treated tolerogenic dendritic cells induces T-regulatory cells that dampen chronic inflammation that could prevent or reverse autoimmune processes.<sup>19</sup> Evidence also suggests that decreased 25(OH)D levels in children and infants are associated with a higher prevalence of respiratory tract infections and that vitamin D supplementation may reduce influenza and acute upper respiratory infections.<sup>20,21</sup>

For those with chronic inflammatory conditions (e.g., celiac disease, IBD, dysbiosis, eczema), daily vitamin D supplementation may be a critical application for enhancing optimal health and quality of life, beyond the goal of repletion. Low concentrations of vitamin D are associated with disrupted immune function in gastrointestinal diseases.<sup>4,22</sup> VDR regulates the innate immune response in the gut, plays a critical role in regulating endothelial tight junction protein expression, and regulates the intestinal microbiota by controlling microflora composition.<sup>4</sup> Animal models demonstrate that inadequate vitamin D production and/or VDR activity in the gut supports the growth of pathogenic bacteria and intestinal inflammation.<sup>4</sup> In a retrospective review of children ages 3-16 with IBD and vitamin D deficiency, 3 months of high dose oral vitamin D<sub>3</sub> supplementation significantly improved inflammatory markers and disease activity scores associated with IBD, significantly increased 25(OH)D levels, and normalized serum calcium levels.<sup>23</sup> Anxiety and mood disorders have the ability to weaken the immune system. In diabetic females with anxiety and vitamin D deficiency, high-dose supplementation every two weeks for 4 months significantly improved mood status, decreased high-sensitivity C-reactive protein levels, and increased the anti-inflammatory cytokine interleukin-10 in serum.<sup>24</sup>

## Supplement Facts

Serving Size 1 capsule

Amount Per Serving	% Daily Value	
Vitamin D (as Cholecalciferol)	125 mcg (5000 IU)	625%
Vitamin K (as Vitamin K1 Phytonadione 500 mcg; Vitamin K2 Menaquinone-7 50 mcg)	550 mcg	458%

**Other Ingredients:** Microcrystalline cellulose, cellulose (capsule), L-leucine.

### Recommended Use:

- Take one capsule per day with a meal, or as directed by your health care practitioner.

**Note:** Individuals take more than 2,000 IU vitamin D per day should have their vitamin D blood levels monitored by their health care practitioner.

**Warning:** Consult your health care practitioner before using this product if you are taking Coumadin, warfarin or other anticoagulant medications.

For a list of references cited in this document, please visit:

<https://www.designsforhealth.com/techsheet-references/vitamin-d-supreme-references.pdf>

Dosing recommendations are given for typical use based on an average 150 pound healthy adult. Health care practitioners are encouraged to use clinical judgement with case-specific dosing based on intended goals, subject body weight, medical history, and concomitant medication and supplement usage.

\*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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