JUSIAK, Justyna, HALIK, Paulina, ZAŁĘSKI , Daniel, KRANKIEWICZ, Michał and BERDZIŃSKA, Martyna. Vitamin D: Role, Sources, Mechanism of Action and Significance for Human Health. Quality in Sport. 2025;47:66791. eISSN 2450-3118.
https://doi.org/10.12775/QS.2025.47.66791
https://apcz.umk.pl/QS/article/view/66791

The journal has been awarded 20 points in the parametric evaluation by the Ministry of Higher Education and Science of Poland. This is according to the Annex to the announcement of the Minister of Higher Education and Science dated 05.01.2024, No. 32553. The journal has a Unique Identifier: 201398. Scientific disciplines assigned: Economics and Finance (Field of Social Sciences); Management and Quality Sciences (Field of Social Sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398. Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).
The authors declare that there is no conflict of interest regarding the publication of this paper.
Received: 21.11.2025. Revised: 26.11.2025. Accepted: 26.11.2025. Published: 30.11.2025.

Vitamin D: Role, Sources, Mechanism of Action and Significance for Human Health

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Abstract

Introduction.

Vitamin D is a key micronutrient regulating calcium–phosphate homeostasis, immune responses, and several extra-skeletal functions. Its active form, 1,25-dihydroxyvitamin D, acts via the vitamin D receptor present in numerous tissues.

Materials and methods.

A literature review was conducted using PubMed, Dove Press Medical, and Google Scholar. Studies concerning the sources, metabolism, mechanisms of action, and health effects of vitamin D were analyzed.

Results.

Vitamin D supports calcium absorption and bone mineralization, and supplementation of 800–1000 IU/day may reduce fracture risk in deficient individuals. It modulates innate and adaptive immunity by influencing cytokine production and the activity of T and B lymphocytes and macrophages. Deficiency is linked to increased susceptibility to infections, including tuberculosis and viral respiratory illnesses. Research also suggests associations between low vitamin D levels and autoimmune diseases, depression, and cancer, although intervention studies show inconsistent outcomes.

Discussion.

The reviewed evidence confirms the broad physiological effects of vitamin D; however, uncertainties remain regarding optimal dosage and its extra-skeletal benefits. Variability in clinical results may reflect differences in baseline 25(OH)D levels, study populations, and supplementation regimens.

Conclusions.

Vitamin D supplementation appears most beneficial for individuals with documented deficiency, whereas its preventive or therapeutic impact in the general population is less clear. Further high-quality studies are needed to establish optimal dosing and clarify its role in chronic and immune-related diseases.

Keywords

vitamin D, osteoporosis, cancer, autoimmune diseases, nfections, mental health

Introduction

Vitamin D is a fat-soluble vitamin that can be obtained from dietary sources or produced naturally by the body when the skin is exposed to sunlight. There are two main forms of vitamin D (calciferol):
Vitamin D2 (ergocalciferol) – sources include mushrooms and dairy products
Vitamin D3 (cholecalciferol) – sources include animal-derived products such as eggs, meat and fish.

Both forms of vitamin D are absorbed in the small intestine. It has been shown that vitamin D2 is equivalent or slightly less effective than vitamin D3 in achieving optimal serum levels of 25-hydroxyvitamin D (25(OH)D). Another source of vitamin D is synthesis in the skin upon exposure to ultraviolet B (UVB) radiation. It is estimated that dermal synthesis accounts for approximately 90% of the total vitamin D present in the human body. Exposure to UVB radiation (wavelength 290–315 nm) causes the conversion of 7-dehydrocholesterol in the epidermal cells of the skin into previtamin D3, which further isomerises into vitamin D3.

Vitamin D obtained from the diet and skin is metabolized in the liver to 25-hydroxyvitamin D, which is used to assess the vitamin D status in patient serum. Subsequently, 25(OH)D is metabolized in the kidneys and liver, with the involvement of cytochrome P450 and the enzyme 25-hydroxyvitamin D-1α-hydroxylase, into its active form – 1,25-dihydroxyvitamin D (calcitriol, 1α,25$(OH)_2$D) [1,2,3,4].

The active hormone binds to the vitamin D receptor (VDR), forming a complex that dimerizes with the retinoid X receptor (RXR) and is subsequently translocated to the nucleus. Within the nucleus, the heterodimer binds to vitamin D–responsive elements (VDREs) in the promoter regions of vitamin D–responsive genes and induces their expression. Vitamin D exerts its effects by binding to the VDR in the intestines, where it stimulates calcium absorption, and in bone, where it promotes osteoblast differentiation and matrix mineralization. However, VDR is also present in other tissues such as bone marrow, brain, colon, breast and malignant cells and immune cells, suggesting that vitamin D may have additional functions throughout the body. [5]

Materials and methods

Scientific papers published between 2007 and 2025 were analyzed from databases such as PubMed, Dove Press Medical, and Google Scholar, focusing on the topic "Vitamin D: Role, Sources, Mechanism of Action, and Significance for Human Health".

Keywords: vitamin D, osteoporosis, cancer, autoimmune diseases, infections, mental health

Results

Role of Vitamin D in the Body

The role of vitamin D and its effects on the human body have recently become the focus of numerous studies, particularly regarding the regulation of bone mineralization, immune response to infections and mental health [1].

Calcium Homeostasis and Bone Health

Vitamin D plays a crucial role in calcium absorption and bone mineralization. The active form, 1,25-dihydroxyvitamin D, promotes calcium absorption in the intestines, which increases bone mineral density (BMD) through efficient mobilization of bone minerals.

The effect of $1\alpha,25(OH)_2D$ on osteogenic cells is multifaceted, potentially leading to both bone resorption and formation. Vitamin D supports osteoclastogenesis by binding to the VDR receptor in osteoblasts, increasing the expression and release of RANKL ligand. This action raises the RANKL/osteoprotegerin (OPG) ratio, promoting bone resorption [6].

One study conducted in a cohort of individuals receiving vitamin D supplementation at a dosage of 800–1000 IU demonstrated a significantly reduced risk of osteoporotic fractures. It was further established that dosages below 800 IU or above 1000 IU do not exert a statistically significant effect on fracture risk. Additionally, patients with vitamin D deficiency exhibited a marked reduction in fall risk following supplementation, which may be attributable to improvements in muscle mass and strength compromised by the deficiency.[7]

Another study aimed at determining volumetric bone mineral density (BMD) and bone strength in relation to the dose of vitamin D supplementation included three dosages: 400 IU, 4000 IU and 10 000 IU. The study demonstrated that while vitamin D supplementation provides certain overall benefits, no proportional increase in BMD was observed with higher doses.[8]

The aim of another study was to determine whether a monthly single dose of 60,000 IU of vitamin D affects the reduction in fracture incidence. A slight effect of vitamin D supplementation on lowering fracture frequency was demonstrated.[9]

In summary, vitamin D plays a key role in maintaining and regulating bone homeostasis; however, the optimal dosage to reduce fracture risk has not yet been clearly established.[9,10]

Immune Functions

Vitamin D is crucial for the proper functioning of the immune system. Studies indicate that it significantly contributes to protection against bacterial and viral infections [11].

The active metabolite, $1\alpha,25(OH)_2D$, binds to the VDR receptor to form the ligand–receptor complex (Vit D–VDR). This complex initiates the transcription of genes responsible for the production of proteins involved in the anti-inflammatory effects of vitamin D. The Vit D–VDR complex modulates the immune response, influencing the differentiation of immune cells such as B lymphocytes, T lymphocytes, and macrophages [1,12,13].

Vitamin D also induces the transcription of antimicrobial peptides, including cathelicidin and defensin β2, in bone marrow cells, monocytes, macrophages, and neutrophils. Additionally, it regulates the production of proinflammatory cytokines [1].In one study conducted on a group of patients hospitalized in the Intensive Care Unit due to COVID-19 infection, it was shown that supplementation with an initial weekly oral dose of 60,000 IU of vitamin D3, followed by a daily maintenance dose of 5,000 IU, led to an increase in the number of lymphocytes and natural killer (NK) cells. [14]

For instance, a study conducted among postmenopausal women who began vitamin D supplementation assessed immunological and inflammatory markers. Oral supplementation with 1000 IU of Vit D3 resulted in a decrease in levels of IL-5, IL-6, IL-12p70, IL-17α, TNF-α, and interferon-gamma [15].

The aim of another study was to assess the effect of high doses of vitamin D_3 (VD_3) – 50,000 IU per week – on selected circulating cytokines associated with cytokine storms in adults with vitamin D deficiency. It was demonstrated that vitamin D_3 supplementation significantly increased serum levels of IL-6, IL-1β, and IL-10.[12]

It was also shown that 25OHD levels are lower in patients with various inflammatory diseases. Furthermore, the findings regarding the effects of vitamin D_3 supplementation on inflammation, including cytokine alterations, were inconsistent.[12]

Health Effects of Vitamin D

Infections

The role of vitamin D in the development and progression of chronic diseases has been widely investigated in recent scientific literature. The deficiency of this vitamin is linked to greater susceptibility to infectious diseases. In a study involving 67 patients with moderately advanced tuberculosis lesions, the addition of vitamin D supplementation to standard anti-tuberculosis therapy was associated with improved clinical outcomes. Patients receiving vitamin D exhibited a significantly higher rate of sputum conversion as well as marked radiological improvement compared with those receiving standard treatment alone. [5, 16, 17]

Another study was conducted to investigate whether serum concentrations of 25(OH)D were associated with the incidence of acute viral respiratory tract infections. In a cohort of 198 healthy adult participants, it was found that individuals with serum 25(OH)D levels ≥ 38 ng/mL had a significantly lower risk of developing acute viral respiratory infections compared with those who had lower vitamin D concentrations [18]. In line with these observations, numerous studies have demonstrated that vitamin D supplementation can significantly reduce the risk of influenza infections. [19]

Autoimmune diseases

Vitamin D exerts regulatory effects on various immune cells, which has prompted growing interest in investigating its potential role in the prevention and management of autoimmune diseases. Clinical studies have demonstrated a correlation between vitamin D deficiency and an increased prevalence of autoimmune conditions such as systemic lupus erythematosus, rheumatoid arthritis, and multiple sclerosis. However, evidence regarding the effects of vitamin D supplementation on disease activity and progression remains inconsistent and requires further investigation [5, 20, 21, 22,27].

Mental health

Depression is one of the most common psychiatric disorders worldwide. Due to its increasing prevalence in the population, numerous studies have been conducted in recent years to explain the causes of this condition. It has been shown that the development of depression is influenced by factors such as genetic predisposition, cognitive dysfunctions, stressful life events, and interpersonal difficulties. Research in nutritional psychiatry also suggests that dietary factors *such as vitamin D supplementation* may play a significant role both in the development of depression and in alleviating its symptoms [23].

Cancer

The role of vitamin D in cancer has been increasingly investigated. The studies document that 1,25-dihydroxyvitamin D exerts antitumor effects, primarily through the induction of apoptosis and cellular differentiation, along with the suppression of cell proliferation, inflammatory signaling, angiogenesis, invasion, and metastatic progression. Vitamin D modulates these pathways in a differential manner between normal and tumor cells, a feature that may represent a crucial role in its potential therapeutic application in cancer treatment. Furthermore, studies indicate that the addition of vitamin D to standard anticancer therapies can enhance treatment efficacy [24,25]. Additionally, low serum 25(OH)D concentrations have been associated with reduced cancer mortality, whereas available studies have not shown a statistically significant reduction in overall cancer incidence with vitamin D supplementation, highlighting the need for further investigation [26].

Discussion

The results of the presented studies confirm the complex and multidirectional effects of vitamin D on human physiology, encompassing both the regulation of calcium–phosphate homeostasis and the modulation of immune responses. Despite the well-established mechanisms of synthesis, metabolism, and action of calcitriol, many uncertainties remain regarding the optimal supplementation dosage, the effectiveness of different forms of vitamin D, and its extra-skeletal functions.

In the context of bone health, recent studies indicate that moderate doses of vitamin D (800–1000 IU per day) may reduce the risk of osteoporotic fractures, particularly in individuals with vitamin D deficiency and in older populations.

The analysis of the immunological functions of vitamin D confirms its significant influence on inflammatory responses and on both innate and adaptive immunity. The active metabolite, $1,25(OH)_2D$, affects various immune cell populations -including T lymphocytes, B lymphocytes, and macrophages -modulating their activity and regulating the expression of pro- and anti-inflammatory cytokines. However, clinical findings remain inconsistent. Some studies have demonstrated beneficial effects of supplementation, such as reductions in pro-inflammatory markers including IL-6 and TNF-α, while others have reported increases in selected cytokines, particularly when high doses (50,000 IU weekly) were used. This may suggest that the immune response to supplementation depends on baseline 25(OH)D levels, the patient's health status, age, dosing regimen, and duration of therapy.

The presented findings confirm that vitamin D plays an important role in regulating the immune response and may influence the course of certain chronic diseases. The clinical improvement observed in patients with tuberculosis following vitamin D supplementation suggests that its use may support the effectiveness of standard therapy.

According to available literature, higher concentrations of 25(OH)D are also associated with a lower risk of viral respiratory tract infections, which is reflected in studies on influenza. These results highlight the immunomodulatory properties of vitamin D, although the effectiveness of supplementation remains variable and depends on many factors, such as dosage and baseline 25(OH)D levels.

The role of vitamin D in autoimmune diseases and depression is a promising yet still inconclusive area of research. Although vitamin D deficiency is more frequently observed in individuals with these conditions, current interventional studies do not provide definitive evidence that supplementation effectively reduces symptoms or slows disease progression.

Conclusions

Overall, vitamin D supplementation appears to be most beneficial in individuals with deficiency, whereas in populations with normal baseline levels the effects are considerably weaker or absent. At the same time, the potential role of vitamin D in the prevention of chronic and immune-related diseases remains a topic of ongoing discussion. It is important to consider that factors such as sun exposure, diet, age, chronic diseases, and obesity may significantly influence serum 25(OH)D levels and the body's response to supplementation.

Author's contribution

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Funding acquisition: not applicable.
All authors have read and agreed with the published version of the manuscript.
Founding Statement: The study did not receive funding.
Institutional Review Board Statement: Not applicable.
Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflict of Interest Statement: The authors declare no conflicts of interest.

Acknowledgments: Not applicable

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