

# Review on Vitamin D Tablet in Health and Disease Overview

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## ABSTRACT

This review aims to provide an overview of the current understanding regarding the relationship between muscle function and vitamin D. For many years, the molecular mechanisms of vitamin D's action on muscle tissue have been understood to involve both genomic and non-genomic effects. 1,25-dihydroxyvitamin D<sub>3</sub> (1,25(OH)<sub>2</sub>D) binds to its nuclear receptor to start the genomic effects, which alter messenger RNA gene transcription and consequently protein synthesis. The membrane-bound vitamin D receptor (VDR) mediates the quick non-genomic effects of vitamin D. The significance of VDR polymorphisms in the development of osteoporosis and genetic variations in the VDR are still up for debate disagreement and discussion. VDR polymorphisms have most recently been reported to have an impact on muscle function. The body gets 80–100% of the vitamin D it needs from the skin, which has a huge capacity for producing the nutrient. The generation of vitamin D in the skin can be significantly impacted by age, latitude, time of day, and pigmentation. Elderly people in northern latitudes frequently have hypovitaminosis D. Elemental calcium is generally advised for people who are deficient in calcium and vitamin D since it lowers hip fractures and other non-vertebral fractures. Considering the close relationship between high parathyroid hormone levels, low serum calcium, and vitamin D deficiency.

**KEYWORDS** – Muscle Function, Non-vertebral fractures, Vitamin D, Bone health, Osteoporosis.

## INTRODUCTION – [1,2,3]

Among older people, IP fractures are the most dangerous and expensive type of fractures. First of all Falls are a factor in over 90% of hip fractures. Fall-related fractures affect roughly 5% of each year in older individuals, with 1-2% impacting the hip. Because they are more exposed, subjects who experience repeated falls are the most fragile and most likely to have a fracture. Research using long-term vitamin D and calcium supplementation has demonstrated a considerable reduction in non vertebral fractures (32% and 58%) supplementation (18 and 36 months) in older people living in communities and institutions.

The authors from both groups described the results to the noted mild a rise in BMD, or bone mineral density. Alternatively said, these supplements may have an impact on variables that are directly linked to the risk of falls. There is evidence from laboratory, clinical, and epidemiologic studies that vitamin D has a direct impact on muscle strength. Low levels of vitamin D have been linked to reversible myopathy in patients with uremia and osteomalacia. Apart from its impact on calcium homeostasis, vitamin D binds to certain 1,25-dihydroxyvitamin D receptors on skeletal muscle. It was found that older osteoporotic women treated with 1- $\alpha$ -hydroxyvitamin D for three months showed an increase in the relative number and cross-sectional area of fast-twitch muscle fibers in their biopsy specimens.

Our theory was that calcium supplementation and vitamin D would influence calcium homeostasis and improve muscle strength, both of which would lower the chance of falling. If this is the case, vitamin D would improve musculoskeletal function and increase calcium homeostasis, both of which would reduce fractures. This was investigated in a randomized, double-blind study comparing the average number of falls and recurrent falls per year between calcium treatment alone and calcium with vitamin D. Changes in musculoskeletal function and biochemical indicators of bone metabolism were the secondary goals.

Only a small number of clinical trials have been conducted in this area, despite the fact that potential interactions between vitamin D status and muscle function have been known for decades. In light of recently published studies examining the effects of vitamin D and/or calcium treatment on parameters of muscle function or falls, the purpose of this review is to provide an overview of the molecular and clinical perspective of vitamin D action on muscle function. The causes, effects, and additional role of parathyroid hormone are discussed, along with the molecular aspects of vitamin D metabolism and deficiency. Lastly, a discussion of the effects of calcium and vitamin D supplements opens new perspectives on the extra skeletal aspects of vitamin D.

## **HISTORY – [4,5,6]**

Prior to 1890, it was observed that children in Europe who were raised near the coast, where there was more access to sunlight and clean air, showed less evidence of stunted skeletal growth and bowing of weight-bearing bones than children who were raised in cities. Pick's disease is characterized by a progressive thickening of the membranes surrounding the heart, spleen, and liver. Niels Ryberg Finsen, a native of the Faroe Islands (south of Iceland) and an 1890 medical graduate of the University of Copenhagen, suffered from this illness.

He thought that the lack of sunlight in his north-facing home was the cause of his increasing ascites and fatigue. With a strong belief in the benefits of sunlight that have not yet been fully explored, he began collecting data on animals seeking it from his early position as an anatomy tutor. Finsen showed through basic experiments that solar radiation and an electrical arc could have potent antimicrobial properties and improve tissue integrity. He provided compelling evidence of its benefits for patients with smallpox and lupus vulgaris, or skin tuberculosis, which at the time was spreading epidemically throughout Europe.

Finsen quickly gained notoriety as the Nobel Prize was awarded to the father of phototherapy in 1903. Alongside other Nobel laureates who, in the first ten years of the twentieth century, significantly contributed to the development of modern medicine, such as Emil von Behring in 1901 for serum therapy, Ronald Ross in 1902 for malaria infection, Ivan Pavlov in 1904 for the physiology of digestion, and Robert Koch in 1905 for tuberculosis research, his name was immortalized. Phototherapy clinics

treating chronic infectious diseases (primarily tuberculosis) and rickets emerged in sunny regions like the high altitude states of Michigan and the high altitudes of the Alps.

One such instance is the Battle Creek Sanatorium, a health resort that John Harvey Kellogg rebuilt in 1902 following a devastating fire and served as a permanent disability center for veterans of the American wars.

With just two letter changes, "sanatorium" became "san-itarium," and the English language gained a new word that emphasizes wellness. CW Post, the creator of Post Cereals, Amelia Earhart, the first female pilot across the Atlantic, Johnny Weissmuller, the actor known for playing Tarzan, Henry Ford, and Mary Lincoln, the wife of President Lincoln, were among the famous patients treated by the phototherapy and thermotherapy department, which housed the first electric light bath. It was quickly found that glass filtered out the sun's "health" benefits and that sun exposure was just as effective in treating rickets as cod liver oil. (Today, we know that the  $\alpha$ -fraction of ultraviolet (UV) light needed to activate the precursors of vitamin D is neutralized by glass.)

Due to space constraints, not all of the research teams that contributed to the lengthy history leading up to the discovery of vitamin D can be acknowledged. An important experiment was carried out in 1922. They demonstrated that heated cod liver oil maintained its ability to treat rickets in rats but lost its anti-xerophthalmic effect, which was known to be the result of a factor A (later named vitamin A). Given that the water-soluble components identified at the time were referred to as vitamin B and vitamin C, the anti-scurvy factor, they gave the newly disclosed factor the name Vit D. Adolf Windaus, a Berlin-trained physician and 1928 Nobel Prize laureate, focused his scientific career on sterol biochemistry and found a plant steroid in ergot (mushrooms) that, when administered intraperitoneally, cured rickets in rats.

Windaus and other research teams purified the irradiated ergosterol product, which they called vitamin D<sub>2</sub>. At sub-microgram concentrations, it showed strong anti-rachitic effects. Still, one query remained. There is no ergosterol in human tissue. How can exposure to sunlight provide humans with the active form of vitamin D. Long after receiving their Nobel Prize, Windaus and Bock<sup>6</sup> identified 7-dehydrocholesterol in the skin of multiple species in 1937 after arduous work. This material, which was also found in liver and whole milk, was radiation-transformed into an anti-rachitic agent. The product of the radiation was called cholecalciferol, or vitamin D<sub>3</sub>. Vellus et al. deciphered the full photochemical reaction between ergosterol and cholecalciferol in 1955.

## VITAMIN D PRODUCTION <sup>[7,8,9,10]</sup>

It is not an enzymatic process that produces vitamin D<sub>3</sub> (D<sub>3</sub>) in the skin. D<sub>3</sub> (cholecalcitriol/7-DHC) is produced in two stages. First, UV light (spectrum 280–320 UVB) from the sun breaks the B ring, forming pre-D<sub>3</sub>, which isomerizes to D<sub>3</sub> in a process that is noncatalytic but sensitive to temperature. 7-dehydroxy is the source of Calciferol.

The rate at which D<sub>3</sub> forms is influenced by both the intensity of UVB rays and the level of skin pigmentation. Sunscreen and clothing, along with melanin in the skin, prevent UVB rays from reaching 7-DHC, thereby limiting the production of D<sub>3</sub>. The amount of time throughout the year that one can depend on solar exposure to produce D<sub>3</sub> decreases with distance from the equator because UVB intensity from sunlight varies with season and latitude. Dietary sources of vitamin D are also available. Unless fortified, most foods apart from fatty fish don't contain much vitamin D.

Fish contains vitamin D<sub>3</sub>, but fortified foods typically contain D<sub>2</sub>. UVB radiation causes the ergosterol in plants and fungi (like mushrooms) to produce D<sub>2</sub>. It is distinct from D<sub>3</sub> in that it has a methyl group

at C24 in the side chain and a double bond between C22 and C23. D2 is regarded as the original analog of vitamin D. These side chain differences from D3 cause it to have a lower affinity for DBP, which leads to a quicker clearance from the bloodstream. It also restricts the conversion of DBP to 25 hydroxyvitamin D (25OHD) by some of the 25-hydroxylases that will be discussed, and changes the way that DBP is catabolized by 24-hydroxyase. Consequently, D2 supplementation does not raise blood levels of 25OHD as much as comparable amounts of D3 unless it is taken daily.

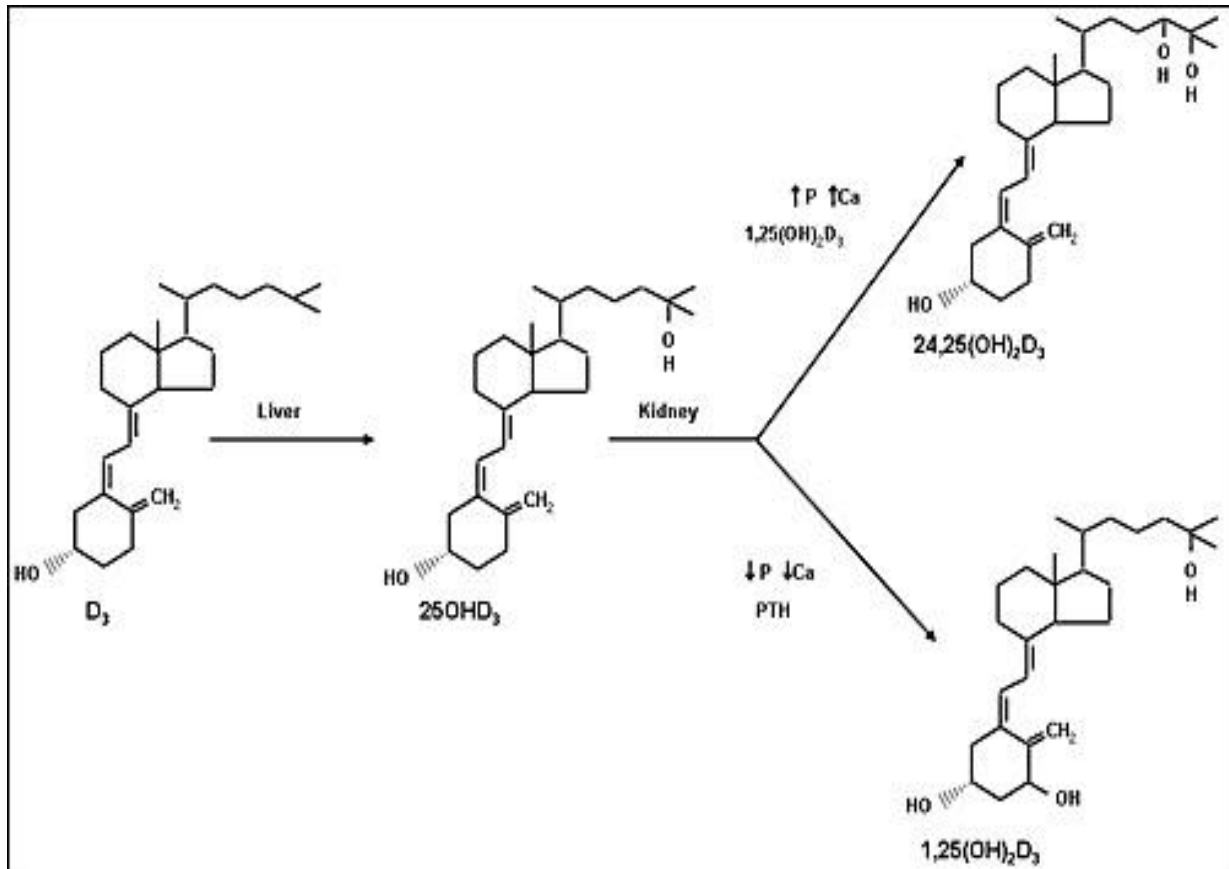


Fig No.1 – Vitamin D Production

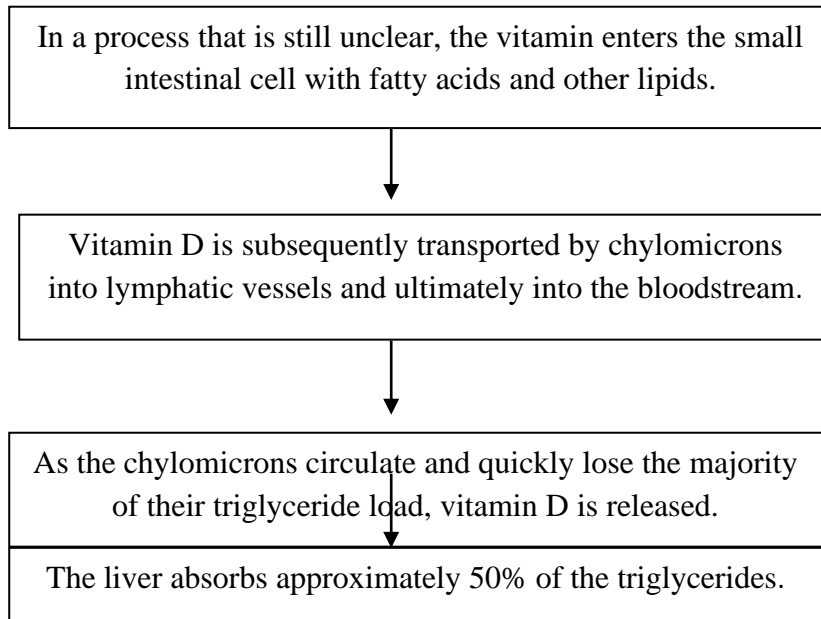
## PHARMACOKINETIC STUDY OF VITAMIN D –

### 1. Vitamin D Absorption –<sup>[11]</sup>

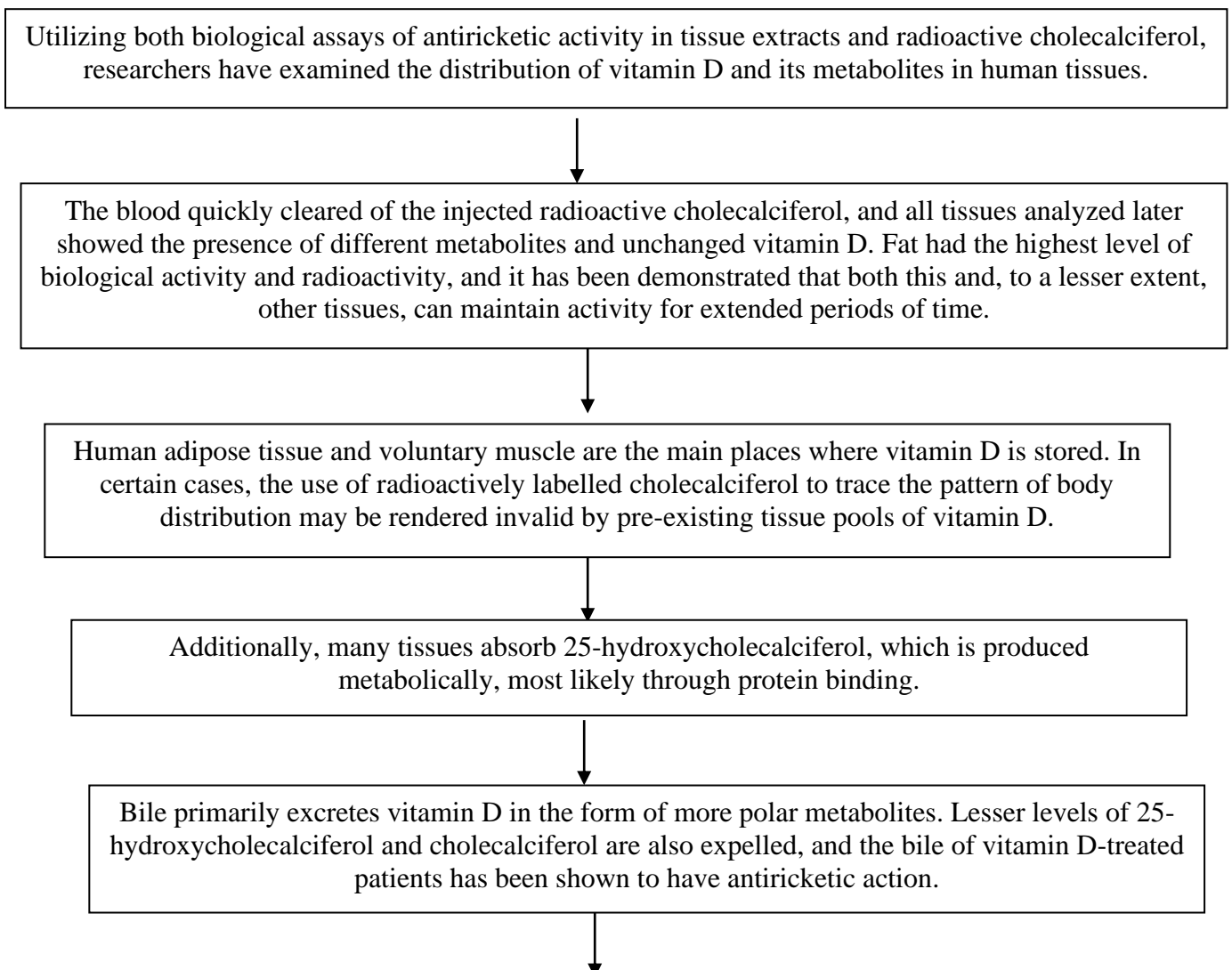
#### Digestion and absorption

Due to its high fat solubility, vitamin D is involved in the formation of mixed micelles during the breakdown of fat, which are primarily made up of phospholipids, fatty acids, monoglycerides, and bile acids.

The majority of the vitamin D that is consumed is absorbed.



## 2. Vitamin D Distribution - [12]



The physical and chemical processes of cholecalciferol (or 25-hydroxycholecalciferol) binding to tissue proteins and partitioning into tissue lipid appear to be responsible for removing an excess of the compound from the blood. It is hypothesized that elevated liver concentrations of vitamin D or 25-hydroxycholecalciferol also result in increased biliary excretion of these substances as well as increased hepatic production and removal of the vitamin's more polar metabolites.

### 3. Vitamin D Metabolism <sup>–[13]</sup>

After being exposed to UVB radiation, the skin produces the secosteroid hormone vitamin D. Eighty to one hundred percent of the body's vitamin D needs are met by the skin, which has a huge capacity for producing the vitamin. Since vitamin D<sub>2</sub> may be less readily converted to 1,25(OH)<sub>2</sub>D than vitamin D<sub>3</sub>, its biologic potency in humans is unknown. Vitamin D<sub>3</sub> is found in fatty fish and is made in the skin. Vitamin D<sub>2</sub> is derived from yeasts and plants.

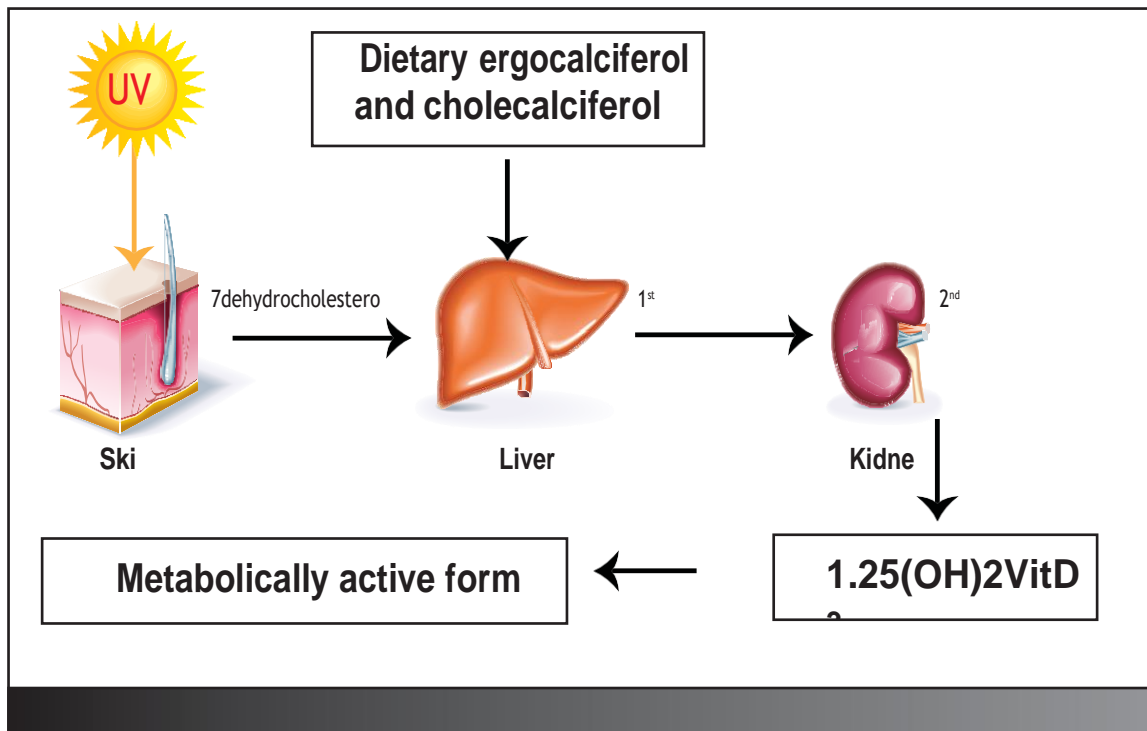
To become the physiologically active 1,25(OH)<sub>2</sub>D, vitamin D must go through two consecutive hydroxylations in the liver and kidney. In the liver, 25-hydroxylation occurs extremely quickly and nearly uncontrollably. Therefore, serum 25-hydroxyvitamin D (25OHD) can be used as a marker for vitamin D status because it reflects both dietary intake and cutaneous production in the skin. However, parathyroid hormone and 1,25(OH)<sub>2</sub>D itself, acting as a negative feedback regulation, tightly control the formation of 1,25(OH)<sub>2</sub>D in the kidney. Prolactin, growth hormone, calcium, and phosphate are additional regulators.

Although the VDR has a 500–1000-fold greater affinity for 1,25(OH)<sub>2</sub>D than for 25OHD, biological activity of 25OHD cannot be completely ruled out due to its roughly 500–fold higher serum concentration. The 24-hydroxylation of 25OHD and 1,25(OH)<sub>2</sub>D results in the formation of 24,25(OH)<sub>2</sub>D and 1,24,25(OH)<sub>3</sub>D, respectively. These metabolites represent the initial stage of the biodegradation process, which culminates in the formation of water-soluble calcitric acid following multiple hydroxylations. Despite the identification of over 40 distinct metabolites of vitamin D, the majority of its biologic actions are thought to be primarily attributed to 1,25(OH)<sub>2</sub>D.

#### Metabolic Activation –

This essay is not intended to be a comprehensive description of the biochemical mechanisms by which vitamin D is activated. However, the figure 1 diagram makes it evident that the activation proceeds through a multi-step process that includes skin UV irradiation and two stages of hydroxylation that result in 1,25(OH)<sub>2</sub> vit D (vit D<sub>3</sub>) in the kidney and liver, respectively, and 25(OH) vit D (vit D<sub>2</sub>). Vitamin D<sub>3</sub> is the metabolically active form. Vitamin D is a fat-soluble substance that has a short half-life as 1,25(OH)<sub>2</sub> vit D and a half-life of roughly three weeks as the 25(OH) vit D stage.

Because of its fat solubility, obese people need higher dosages than people with a normal body fat composition in order to achieve normal blood levels.



**Fig No. 2 - Activation of Vitamin D**

#### 4. Vitamin D Elimination <sup>–[14]</sup>

Cholecalciferol, also known as vitamin D, is a lipophilic secosteroid hormone. Vitamin D levels are sustained by ultraviolet light exposure-induced de novo synthesis in the basal layers of the epidermis or by dietary consumption. As a prohormone, vitamin D needs to be hydroxylated in two steps: first by vitamin D 25-hydroxylase, which produces 25(OH)D, and second by vitamin D 1- $\alpha$ -hydroxylase1, which produces 1,25 dihydroxyvitamin D, which is the most polar and bioactive vitamin D metabolite (1,25(OH)<sub>2</sub>D). The primary circulating form of vitamin D, 25(OH)D, is currently thought to be the best indicator of vitamin D status in the body due to the short half-life of 1,25(OH)<sub>2</sub>D in plasma.

The biological activity of 1,25(OH)<sub>2</sub>D is mediated through its binding to and activation of the vitamin D receptor (VDR). It has been demonstrated that the regulatory complex formed by the liganded VDR heterodimerizing with the retinoid X receptor, or in some cases the retinoic acid receptor, controls the expression of up to 3% of the transcribed genome in target cells. Insufficient levels of vitamin D are common in the human population, with more than A billion individuals globally impacted. According to epidemiological data, patients with cardiovascular disease frequently have vitamin D deficiency. Lower plasma 25(OH)D levels have been linked to a higher risk of myocardial infarction, ischemia heart disease, hypertension, and early death. Six Researchers have demonstrated that vitamin D therapy improves endothelial function, lowers blood pressure, and reverses cardiac hypertrophy in humans in a few interventional studies. These clinical findings provide credence to the idea that low vitamin D is a risk factor for cardiovascular disease development and that raising vitamin D levels can reduce this risk.

#### MECHANISM OF ACTION OF VITAMIN D <sup>–[15,16,17]</sup>

The VDR mediates all of 1,25(OH)<sub>2</sub>D's genomic actions. VDR belongs to the nuclear receptor family of steroid hormones and functions as a transcription factor. It is made up of three domains: the C-terminal ligand binding domain, the hinge region that connects the two N-terminal DNA binding domains

together, and the two zinc fingers that bind to the DNA grooves at discrete sites (VDREs). X-ray crystallography has been used to solve the structure of the ligand binding domain.

The terminal helix facilitates the interaction between VDR and its heterodimer partner, usually RXR, by acting as a gating mechanism that closes around the incorporated ligand and forms an interface for coactivators. While VDRE sequences vary widely, the majority of those that have the strongest affinity for VDR are essentially direct repeats of hexanucleotides that have three nucleotides between the half sites a motif known as a DR3. Following VDR binding to its VDRE, coregulatory complexes needed for its genetic operations. The selectivity of 1,25(OH)<sub>2</sub>D action from one cell type to another is made possible by these complexes, which can be both gene- and cell-specific. Several subunits with enzyme activity, such as histone acetyl transferases (coactivators like the SRC family) or deacetylases (corepressors like SMRT and NCoR), methyl transferases and demethylases, ATPase-containing nucleosomal-remodeling activity, and links to RNA polymerase II (Mediator complex), are included in these complexes. One subunit directly binds to the VDR via an motif. Our understanding of vitamin D's mechanism of action at the genomic level has significantly increased thanks to the more recent techniques of microarray, ChIP-chip, and ChIP-seq. For instance, after administering 1,25(OH)<sub>2</sub>D, 8,000 VDR binding sites were discovered in the mouse osteoblast as opposed to 1,200 sites under basal conditions. 2,776 VDR binding sites were discovered to be changing the expression of 229 genes in a different study using human lymphoblastoid cell lines treated with 1,25(OH)<sub>2</sub>D.

#### **NORMAL SERUM CONCENTRATIONS** <sup>[18]</sup>

By measuring the serum concentration of 25(OH) vitamin D, vitamin D status is determined. displays the reference ranges and normal concentrations. The minimal ideal serum concentration of 30 ng/ml is not reached by an estimated one billion people globally.<sup>12</sup> Vitamin D supplements shouldn't be recommended unless it has been determined that the serum concentration is inadequate or deficient.

#### **SOURCES OF VITAMIN D** <sup>[19]</sup>

While the body synthesises and activates vitamin D as described, there are a number of external sources that can help fulfill the adult requirement of 2000 IU 25(OH) of vitamin D per day without requiring UV activation of 7-dehydro-cholesterol in the skin. Infants who are breastfed ought to get 400 IU daily until they are weaned. Children and teenagers who consume less than 500 milliliters of vitamin D-fortified milk per day are advised to take the same dosage.) The USA Food and Nutrition Board of the Institute of Medicine updates these recommendations on a regular basis. Below is a brief summary of the external sources of vitamin D, which include ergocalciferol and cholecalciferol.

- Cholecalciferol tablets, which come in a variety of dosages up to 50,000 IU each.
- Untamed salmon
- Ergocalciferol-containing mushrooms, especially those that have been exposed to UV
- Mackerel, especially when caught in the wild. The value of breeding in captivity diminishes as a source of vitamin D.
- Cod liver oil (vitamin A toxicity to be aware of) Sardines and tuna
- Yogurt, milk, egg yolks, and the liver of cattle or calf



## VITAMIN D TOXICITY <sup>–[20]</sup>

Because of its complex activation pathway and negative feedback mechanisms, exposure to natural sunlight has not been linked to vitamin D toxicity. However, chronic daily excessive vitamin D intake (of the order of 40,000 IU or more) through oral consumption or UV device use is theoretically capable of causing vitamin D toxicity. On the other hand, not much is known about the consequences (if any) of vitamin D toxicity. The National Institutes of Health arbitrarily set the daily intake of 2000 IU for adults and the maximum upper limit of 25(OH) vitamin D serum concentration at 100 ng/m<sup>TM</sup>. This will definitely be increased because it is said that 30 minutes of full body sun exposure produces 10,000 IU of vitamin D.

## VITAMIN D IN BONE HEALTH <sup>–[21]</sup>

Over the past 70 years, a great deal of research has been done on the traditional function of vitamin D, which is to maintain the calcium balance of the skeleton. The mechanisms involve enhancing the intestinal absorption of calcium and supporting the appropriate function of parathyroid hormone, which in turn sustains fundamental metabolic activities that necessitate sufficient levels of calcium and phosphate in the serum.

The effects of a vitamin D deficiency are widely known and include osteomalacia after skeletal growth has stopped and rickets in children. Readers are referred to other publications for an elaborate discussion of the skeletal biochemical changes associated with vitamin D deficiency.

## CLINICAL APPLICATION –

It is impossible to condense the extensive body of research on the connection between vitamin D deficiency and human disease into a few succinct paragraphs. Still, there are a few things to say about some of the clinical uses that have gotten the most research.

### 1. The Skeleton- <sup>[22,23,24]</sup>

Supplementing with vitamin D and preventing fractures. A reduction in falls linked to vitamin D may account for at least some of the protection. The question of whether vitamin D's beneficial effects on bone are exclusively attributable to its ability to increase intestinal absorption of phosphate and calcium from the diet by means of 1,25(OH)<sub>2</sub>D is still up for debate. Additionally, directly affects bone and cartilage to support healthy skeletal growth and turnover. Rickets is caused by mice and humans who lack a functional VDR , but it can be avoided by infusions of calcium and phosphate or by eating a rescue diet rich in calcium and lactose, which improves calcium absorption. Additionally, it has a direct impact on bone and cartilage to promote normal skeletal turnover and growth. A rescue diet high in calcium and lactose, which enhances calcium absorption, or the infusion of calcium and phosphate can prevent rickets, which is caused in mice and humans lacking a functional VDR.

### 2. The Skin – <sup>[25,26]</sup>

Another authorized clinical use for vitamin D and its analogs outside of the skeleton is the treatment of hyperproliferative skin diseases such as psoriasis with the 1,25(OH)<sub>2</sub>D analogs maxacalcitol and calcipotriol. Psoriasis is a disorder characterized by decreased or aberrant differentiation and hyperproliferation, which is caused by an aberrant immune component.

The ability of 1,25(OH)<sub>2</sub>D and some of its analogs to prevent proliferation, promote differentiation, and reduce immune activity linked to this illness is probably the reason for its successful use. The condition of increased proliferation and decreased differentiation of keratinocytes is also representative of nonmelanoma skin cancer. According to mice deficient in VDR in their keratinocytes are more vulnerable to UVB and chemically induced skin cancer, and topical administration of 1,25(OH)<sub>2</sub>D seems to have photoprotective properties.

### 3. Obesity, Diabetes Mellitus And Metabolic Syndroms – [27,28]

Obese people are more likely to develop diabetes mellitus and the metabolic syndrome, and their 25OHD levels are generally lower in these individuals. According to adipocytes express the VDR, and 1,25(OH)<sub>2</sub>D stimulates both increased lipogenesis and decreased lipolysis. The VDR is expressed by pancreatic b cells, and 1,25(OH)<sub>2</sub>D stimulates the release of insulin. Additionally, insulin resistance and vitamin D deficiency are linked. Longer and larger randomized clinical trials are needed to confirm the benefit of vitamin D administration in treating or preventing the development of frank diabetes in people with diabetes mellitus or prediabetes.

### 4. Cancer – [29,30]

The mechanisms by which 1,25(OH)<sub>2</sub>D can suppress tumor development are numerous and in many cases cell specific. These include inhibition of proliferation by blocking elements of the cell cycle or interference with signaling by growth factors, inducing apoptosis, stimulation of DNA damage repair, prevention of tumor angiogenesis, and inhibition of metastasis. However, most of the clinical data stem from observational studies

These studies repeatedly demonstrate a possible benefit of vitamin D supplementation in cases of colon and breast cancer; however, there are insufficient data from randomized clinical trials that are large enough, long enough, and contain high enough doses of vitamin D to be conclusive.

### 5. Cardiovascular Disease – [31,32,33,34]

In the heart, the fibroblasts and myocytes both VDR. Hypertrophy is caused by deletion of the VDR specifically from the heart, and 1,25(OH)<sub>2</sub>D and its analogs suppress markers of cardiac hypertrophy. According to VDR null mice exhibit hypertension due to elevated renin production from their hearts and kidneys, which raises the levels of angiotensin II in the blood.

But no significant randomized clinical trial has been conducted to date with the express purpose of examining the role of vitamin D or any of its analogs in the prevention or treatment of CVD, and the findings of fracture studies with CVD as a secondary outcome have not been particularly encouraging.

### 6. Immune Function – [35,36,37,38]

Toll-like receptors (TLRs) on polymorphonuclear cells (PMNs), monocytes, macrophages, and several epithelial cells are activated during the innate immune response. The host's innate immune response is triggered by specific membrane patterns (pathogen-associated molecular pattern, or PAMP) released by infectious agents. TLRs are an extended family of noncatalytic transmembrane pathogen-recognition receptors that interact with these patterns. Antimicrobial peptides (AMPs) are induced when TLRs are activated. such as reactive oxygen species (ROS) and cathelicidin, which cause the organism's death. 1,25(OH)<sub>2</sub>D stimulates the expression of cathelicidin in both myeloid and epithelial cells. When a

lipopeptide from an infectious organism, like *M. tuberculosis*, stimulates TLR2 in macrophages, it increases the expression of VDR. When there is enough substrate (25OHD), this leads to the induction of cathelicidin. Thus, the innate immune response is supported by sufficient vitamin D levels.

**BONE DISEASE** – [39,40,41,42,43]

Although low levels of vitamin D are almost always found in cirrhosis patients it has long been questioned whether vitamin D deficiency is a cause of hepatic bone disease significant study in this field found that, in 107 patients, whom had cirrhosis, there was no evidence of osteomalacia on bone biopsy, indicating that bone disease in patients with liver disease was unrelated to their vitamin D status. Conversely, 39% of these patients had osteoporosis, and serum 25-hydroxyvitamin D levels were found to predict forearm bone density but not lumbar spine bone density (hip bone density was not measured). One could argue that the results in these patients support the theory that low bone density is caused by vitamin D deficiency because, historically, bone loss is greater from sites where cortical bone predominates (like the forearm and hip) than from sites where trabecular bone predominates (like the spine). This is because vitamin D deficiency can lead to the development of secondary hyperparathyroidism. It has only been possible to measure hip bone density using dual X-ray absorptiometry for the past 15 years.

Since then, research has demonstrated that the levels of 25-hydroxyvitamin D and 1,25-hydroxyvitamin D are reliable indicators of hip bone density in both postmenopausal women with osteoporosis and patients with cirrhosis. Although patients with cirrhosis have been reported to have osteomalacia linked to secondary hyperparathyroidism, osteomalacia is uncommon and only develops after a protracted and severe vitamin D deficiency. Individuals lacking in vitamin D, especially those whose deficiencies are caused by poor dietary D absorption, may initially prior to the onset of osteomalacia, experience a protracted period of increased fracture risk and secondary hyperparathyroidism.

**VITAMIN D AND MENTAL HEALTH** – [44,45]

Due to their lack of exposure to sunlight, poor dietary habits, use of anticonvulsants, and overrepresentation of ethnic groups known to be at higher risk, psychiatric in-patients may be especially susceptible to vitamin D deficiency. People who struggle with mental health issues frequently have poor physical health, and many of the issues linked to vitamin D deficiency exacerbate pre-existing medical morbidity in this population.

Some writers have proposed that low vitamin D levels may independently predispose individuals to mental disorders due to the epidemiology of vitamin D deficiency and schizophrenia being similar. In a study examining a birth cohort from Northern Finland, it was discovered that males but not females who took vitamin D supplements during the first year of life had a lower chance of developing schizophrenia later in life. Nevertheless, preliminary research has not found any correlation between vitamin D receptor polymorphisms and the risk of schizophrenia.

**MARKETED PREPARTION** –

Sr. No	Name	Brand	Vitamin D Form	Strength	Formulation
1	Adferol	Steadfast Medishield	Cholecalciferol	60,000 IU	Capsules

		Pvt. Ltd			
2	Alfacal	Macleods Pharmaceuticals Ltd.	Alfacalcidol	0.25 mcg	Capsules
3	Alfadol	Panacea Biotech Ltd.	Alfacalcidol	0.5 mcg	Capsules
4	Alfa calcirol	Cadila	Alfacalcidol	0.25 mcg	Capsules
5	Alfacip	Cipla Pharmaceuticals	Alfacalcidol	0.25 mcg	Capsules
6	Alphadol	Panacea Biotech	Alfacalcidol	0.25 mcg	Capsules
7	Alfarich	Cipla Ltd.	Alfacalcidol	0.25 mcg	Capsules
8	Caltive	Intas Pharma	Calcitriol	0.25 mcg	Capsules
9	Caldikind Plus	Mankind Pharma Ltd.	Calcitriol	0.25 mcg	Capsules
10	D rise	US Vitamin Ltd.	Vitamin D3	2000 IU	Softgel Capsules
11	Macbrite D3	Macleods Pharmaceuticals	Cholecalciferol	60,000 IU	Softgel Capsules
12	Bio D3 Plus	Macleods Pharmaceuticals Pvt. Ltd.	Calcitriol	0.25 mcg	Softgel Capsules
13	Gen D3	Macleods Pharmaceutical Ltd. (gencare)	Cholecalciferol	60,000 IU	Softgel Capsules
14	Rocaltrol	Abott	Calcitriol	0.25 mcg	Softgel Capsules
15	Alfa D3	GSK Pharmaceuticals Lts	Alfacalcidol	0.25 mcg	Softgel Capsules
16	Alfa D3	GSK Pharmaceuticals Lts	Alfacalcidol	1 mcg	Softgel Capsules
17	Calcitas D3	Intas Pharmaceuticals Ltd.	Cholecalciferol	60,000 IU	Softgel Capsules

### FUTURE SCOPE-

In order to meet the dietary vitamin D requirements of the general population, even though a number of nutritional vitamin D guidelines have been published in recent years, future tasks include developing and implementing public health strategies (such as requiring food to be fortified with vitamin D). Aiming to address this issue and potentially influencing future public health policies is the EU ODIN project (Food-based solutions for Optimal vitamin D Nutrition and health throughout the life cycle. Hopefully, these initiatives will result in the widespread use of vitamin D food fortification.

Because so many RCTs on vitamin D have recently been published or are soon to be completed, our understanding of its effects is growing dramatically. Large vitamin D RCTs on clinical endpoints that were published did not demonstrate vitamin D's beneficial effects. These results are not surprising given the limitations of these RCTs, which included participants irrespective of their 25(OH)D status and

ignored meta-analyses' findings that the risk of poor health outcomes, like mortality, is only significantly increased at very low 25(OH)D levels.

Plotting the achieved 25(OH)D levels of the placebo and intervention groups onto a 25(OH)D and mortality regression curve does not reveal a meaningful difference in terms of relative risks for, say, mortality, given that the associations of 25(OH)D and some health outcomes show U- or J-shaped relationship. Low response rates, availability of vitamin D supplements, and laboratory testing for 25(OH)D are additional possible drawbacks of these vitamin D trials. These RCTs also have the drawback of evaluating relatively high vitamin D doses rather than the significantly lower doses needed to meet the DRI.

This is concerning, especially in light of the fact that an RCT regarding the risk of falls indicated that a higher vitamin D dosage might potentially be worse than a lower dose. Furthermore, results like those from the EVITA trial, which demonstrated no beneficial effect of three years of vitamin D supplementation on mortality or other clinical endpoints in 400 patients with low levels of 25(OH)D, should be acknowledged and shared as rather obvious results of no effect. In addition, it should be recognized that long-term RCTs are necessary to accurately assess health outcomes like cancer, multiple sclerosis, or Alzheimer's disease; however, these lengthy trials would also raise the risk of dropout and poor adherence. studies using Mendelian randomization that Since they allow us to study lifelong exposure, it is also necessary to assess whether genetically determined variation in 25(OH)D is associated with health outcomes. To sum up this outlook for vitamin D's future, we believe that one of the biggest challenges in the near future will be accurately interpreting vitamin D trials and translating them into possible public health actions and information, especially in light of reports of vitamin D's positive, null, and negative effects.

## CONCLUSION-

Recent research findings provide some support for the theory that low levels of calcium and vitamin D affect muscle function, which in turn raises the risk of falls. However, for those who are deficient in calcium and vitamin D, supplementing with these nutrients may enhance muscle function and lower their risk of falling. However, more investigation is required to pinpoint the precise mechanisms of action given the strong correlation between low serum calcium and high serum levels of parathyroid hormone and vitamin D deficiency. Finding ways to use analogs to target particular cells without also increasing intestinal calcium absorption and/or bone resorption is of great interest. Analogs have been created for the treatment of hyperproliferative skin diseases, hyperparathyroidism, and osteoporosis as a result of this somewhat successful endeavor. However, solid data from randomized clinical trials are lacking for many of the potential applications, including the treatment/prevention of cancer, cardiovascular disease (CVD), infections, and autoimmune diseases, despite encouraging epidemiologic data and animal studies.

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