Calcifediol (Calcidiol, semiactivated Vitamin D) - many studies

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Calcidiol: Prescription typically needed, expensive, probably fast

- Calcidiol supplementation may be be essential to get Vitamin D if there is poor liver function
- Calcidiol is far more expensive than Vitamin D
- Fast Vitamin D response is essential in some cases - such as early COVID

  It appears that Calcidiol provides a fast response (mixed indications)

  Nanoemulsion Vitamin D might also provide a quick response - personal observation, no data yet.

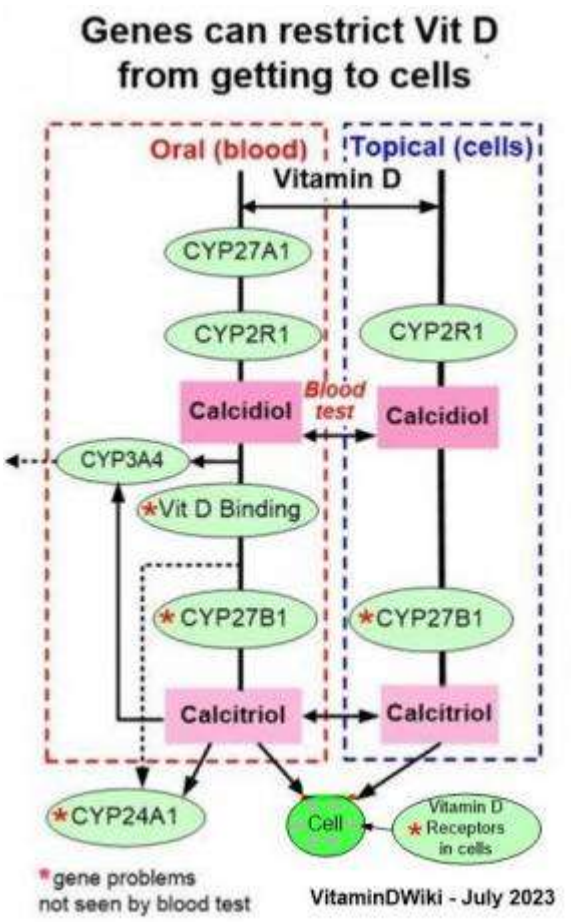
VitaminDWiki - Calcidiol category contains

46 items in Calcidiol category

Calcidiol = Calcifediol = 25-hydroxyvitamin D3 = 25(OH)D = semi-activated Vitamin D

See also

- Tests for Vitamin D 155 items
- Calcitriol 56 items
- Injection 61 items
- Forms of Vitamin D 103 items
- Calcifediol (Calcidiol, semiactivated Vitamin D) - many studies 41 as of Aprol 2023
- Response to Vitamin D - many studies 166 as of April 2023
- Calcifediol is superior to cholecalciferol (it mainly acts faster) – RCT June 2021
- Nanoemulsion Vitamin D is faster and better - many studies
  - Response to Nanoemulstion Vitamin D swished in the mouth appears to start in 2 hours
- Calcidiol is available only by prescription and is expensive
- Calcidiol - daily dose has fast response, but weekly might be better - March 2018



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See COVID related

- Treat COVID early with high-dose Vitamin D (20th as of June 2022)
- Vitamin D might mitigate endemic COVID - June 2022
- Vitamin D also provides COVID Neuroprotection – April 2022
- COVID hospital deaths reduced 2X by 8 days of UVB – pilot RCT May 2022
- Surviving COVID with vitamins and minerals is not a myth – June 2022

COVID-19 treated by Vitamin D - studies, reports, videos

As of Oct 4, 2023, the VitaminDWiki COVID page had: 19 trial results, 37 meta-analyses and reviews, Mortality studies

see related: **Governments, HealthProblems, Hospitals, Dark Skins, All 26 COVID risk factors are associated with low**

Vit D, Fight COVID-19 with 50K Vit D weekly Vaccines Take lots of Vitamin D at first signs of COVID 166 COVID Clinical Trials using Vitamin D (Aug 2023) Prevent a COVID death: 9 dollars of Vitamin D or 900,000 dollars of vaccine - Aug 2023

5 most-recently changed Virus entries

Id	Page	Hits	Last modification
14678	The ONLY Solution to Long COVID (Vitamin D) - video and transcript Sept 2023	931	16 Jan, 2024 09:38
14975	Long-COVID a month shorter if more than 20 ng of Vitamin D - Jan 2024	81	16 Jan, 2024 09:35
13765	Long-COVID is now the biggest COVID concern - many studies	39588	16 Jan, 2024 09:21
14831	COVID infections and vaccinations decrease Vitamin D – many studies	287	15 Jan, 2024 12:07
14481	More psoriasis flares following second COVID vaccination if lowish Vitamin D – May 2023	509	15 Jan, 2024 11:11

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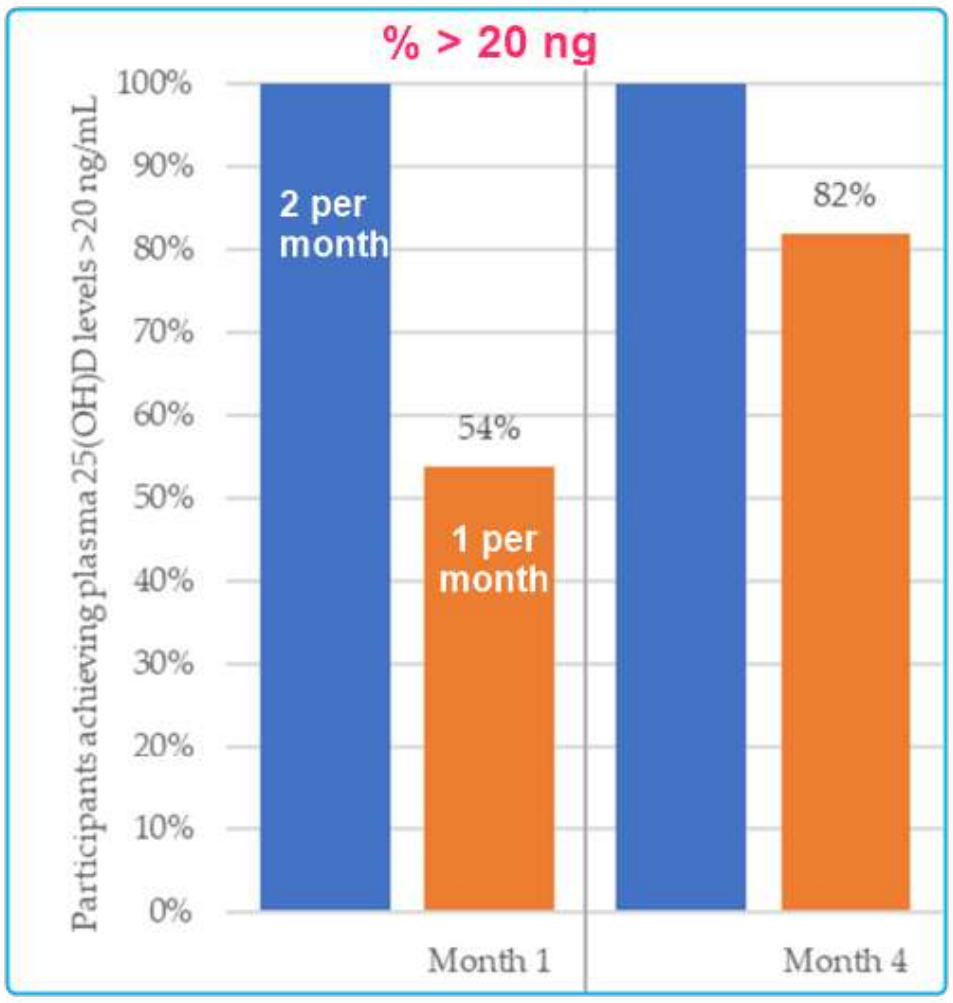
Monthly Calcifediol: >4 months to get to 20ng, bi-weekly just 1 month - Jan 2024

Efficacy and Safety of Calcifediol in Young Adults with Vitamin D Deficiency: A Phase I, Multicentre, Clinical Trial—POSCAL Study

Nutrients Volume 16 Issue 2 10.3390/nu16020306

by Pedro Guerra López 1,Mikel Urroz Elizalde 1,2ORCID,Noelia Vega-Gil 3,Blanca Sánchez Santiago 3ORCID,Iñaki Zorrilla Martínez 4,5,6,7,8,Mario Jiménez-Mercado 4ORCID,Esteban Jódar 9,10,Araitz Landeta Manzano 11,Cristina Campo Hoyos 11,* andJesús Frías Iniesta 1,2

Bi-weekly gets to 20 ng level faster



Vitamin D deficiency is highly prevalent, and recent evidence suggests a possible association between vitamin D deficiency and

various health conditions. The aim of this study was to assess monthly calcifediol treatments for vitamin D deficiency (or biweekly, if the deficiency was severe) in a young adult population with no associated comorbidities. This multicentre phase I trial started with a four month open-label treatment phase (TP) that included 101 participants (65% women with mean age 29.8 years). Eighty-two percent of the subjects (79/96) achieved 25(OH)D levels within the target range (20–60 ng/mL) by the end of the TP, and they were subsequently randomised and subjected to a double-blind, placebo-controlled, five month follow-up phase (FP). At the end of the FP, 89% of participants maintained vitamin D levels of >20 ng/mL with calcifediol, versus 49% with placebo ($p < 0.001$). Subjects receiving monthly calcifediol during both phases (n = 32) maintained 25(OH)D levels >20 ng/mL, whereas those on the placebo during the FP (n = 38) exhibited deficiency levels of 25(OH)D by the end of the study. No clinically relevant changes in bone metabolism parameters or toxic 25(OH)D levels were observed, and no serious adverse events were reported throughout the study. Calcifediol is a safe and effective treatment for vitamin D deficiency in the young adult population, but long-term use may be required to sustain optimal 25(OH)D levels.

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13% of Adverse Events were due to the supplementation (clipped from PDF)

During the study, 66 AEs were reported by approximately one-third (n = 36, 36%) of the safety population (n = 101). Of the total AEs, nine (13.64%) were considered to be potentially related to the study treatment; all of them occurred during the treatment phase, and they were reported by five (5%) participants in the group who were being administered calcifediol each month.

Note: Reponse to Vitamin D does not appear to degrade with monthly dosing

- Vitamin D given daily, weekly, or monthly has similar response (116 RCTs) – meta-analysis Aug 2023
- Vitamin D response independent of dosing interval – meta-analysis July 2023

Cholecalciferol or Calcifediol in the Management of Vitamin D Deficiency - May 2020

Nutrients 2020 May 31;12(6):1617. doi: 10.3390/nu12061617.

Manuel Sosa Henríquez 1 2, M Jesús Gómez de Tejada Romero 3

Vitamin D deficiency is a global health problem due to its high prevalence and its negative consequences on musculoskeletal and extra-skeletal health. In our comparative review of the two exogenous vitamin D supplementation options most used in our care setting, we found that cholecalciferol has more scientific evidence with positive results than calcifediol in musculoskeletal diseases and that it is the form of vitamin D of choice in the most accepted and internationally recognized clinical guidelines on the management of osteoporosis. Cholecalciferol, unlike calcifediol, guarantees an exact dosage in IU (International Units) of vitamin D and has pharmacokinetic properties that allow either daily or even weekly, fortnightly, or monthly administration in its equivalent doses, which can facilitate adherence to treatment. Regardless of the pattern of administration, cholecalciferol may be more likely to achieve serum levels of 25(OH)D (25-hydroxy-vitamin D) of 30-50 ng/mL, an interval considered optimal for maximum benefit at the lowest risk. In summary, the form of vitamin D of choice for exogenous supplementation should be cholecalciferol, with calcifediol reserved for patients with liver failure or severe intestinal malabsorption syndromes.

Conclusions (clipped from PDF)

Based on our current knowledge, treatment of vitamin D deficiency should be aimed to maintain stable and continuous serum levels of 25(OH)D in a range of approximately 30 to 50 ng/mL, which appears to be optimal in terms of maximizing benefits and minimizing risks of vitamin D, regardless of the myriad of genetic and/or environmental factors that may influence the vitamin D status of patients.

In our opinion, and based on the available scientific evidence, cholecalciferol is the form of vitamin D that can ensure that the vast majority of patients with vitamin D deficiency are within the optimal range of efficacy and safety in a long-term period.
Therefore, based on our review of differential pharmacological characteristics and scientific evidence, cholecalciferol should be used and prescribed in the majority of vitamin D deficiency clinical settings instead of calcifediol.

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Calcifediol (25OH Vitamin D3) Deficiency: A Risk Factor from Early to Old Age - March 2022

Nutrients 2022 Mar 10;14(6):1168. doi: 10.3390/nu14061168.

Roger Bouillon 1, Leen Antonio 1 2, Oscar Rosero Olarte 3

Vitamin D deficiency is the main cause of nutritional rickets in children and osteomalacia in adults. There is consensus that nutritional access to vitamin D can be estimated by measuring serum concentrations of 25OHD and vitamin D deficiency can thus be considered as calcifediol deficiency.
However, the threshold for vitamin D/calcifediol sufficiency remains a matter of debate.
Vitamin D/calcifediol deficiency has been associated with musculoskeletal effects but also multiple adverse extra-skeletal consequences. If these consequences improve or if they can be treated with vitamin D supplementation is still unclear.
Observational studies suggest a higher infection risk in people with low calcifediol levels. There is also a consistent association between serum calcifediol and cardiovascular events and deaths, but large-scale, long-term intervention studies did not show any benefit on cardiovascular outcomes from supplementation, at least not in subjects without clear vitamin D deficiency.
Cancer risk also did not change with vitamin D treatment, although there are some data that higher serum calcifediol is associated with longer survival in cancer patients. In pregnant women, vitamin D supplementation decreases the risk of pre-eclampsia, gestational diabetes mellitus, and low birth weight. Although preclinical studies showed that the vitamin D endocrine system plays a role in certain neural cells as well as brain structure and function, there is no evidence to support a beneficial effect of vitamin D in neurodegenerative diseases. Vitamin D supplementation may marginally affect overall mortality risk especially in elderly subjects with low serum calcifediol concentrations.

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Calcifediol prescription may be a good, but expensive way to correct Vitamin D deficiency - June 2023

Calcifediol: a review of its pharmacological characteristics and clinical use in correcting vitamin D deficiency

Eur J Nutr . 2023 Jun;62(4):1579-1597. doi: 10.1007/s00394-023-03103-1

Esteban Jodar 1, Claudia Campusano 2, Renate T de Jongh 3, Michael F Holick 4

Background: In addition to the role of vitamin D in bone mineralization, calcium and phosphate homeostasis, and skeletal health, evidence suggests an association between vitamin D deficiency and a wide range of chronic conditions. This is of clinical concern given the substantial global prevalence of vitamin D deficiency. Vitamin D deficiency has traditionally been treated with vitamin D3 (cholecalciferol) or vitamin D2 (ergocalciferol). Calcifediol (25-hydroxyvitamin D3) has recently become available more widely.

Methods: By means of targeted literature searches of PubMed, this narrative review overviews the physiological functions and metabolic pathways of vitamin D, examines the differences between calcifediol and vitamin D3, and highlights clinical trials conducted with calcifediol in patients with bone disease or other conditions.

Results: For supplemental use in the healthy population, calcifediol can be used at doses of up to 10 µg per day for children ≥ 11 years and adults and up to 5 µg/day in children 3-10 years. For therapeutic use of calcifediol under medical supervision, the dose, frequency and duration of treatment is determined according to serum 25(OH)D concentrations, condition, type of patient and comorbidities.
Calcifediol differs pharmacokinetically from vitamin D3 in several ways.

- It is independent of hepatic 25-hydroxylation and thus is one step closer in the metabolic pathway to active vitamin D.
- At comparable doses to vitamin D3, calcifediol achieves target serum 25(OH)D concentrations more rapidly
- and in contrast to vitamin D3, it has a predictable and linear dose-response curve irrespective of baseline serum 25(OH)D concentrations.

The intestinal absorption of calcifediol is relatively preserved in patients with fat malabsorption and it is more hydrophilic than vitamin D3 and thus is **less prone to sequestration in adipose tissue.**

Conclusion: Calcifediol is suitable for use in all patients with vitamin D deficiency and may be preferable to vitamin D3 for patients with obesity, liver disease, malabsorption and those who require a rapid increase in 25(OH)D concentrations.
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Calcifediol: Why, When, How Much? - April 2023

Pharmaceuticals (Basel) . 2023 Apr 22;16(5):637. doi: 10.3390/ph16050637.
Simone Donati 1, Francesca Marini 2, Francesca Giusti 1, Gaia Palmini 1, Cinzia Aurilia 1, Irene Falsetti 1, Teresa Iantomasi 1, Maria Luisa Brandi 2

Vitamin D deficiency is a constantly growing health problem worldwide. Adults affected with hypovitaminosis D could experience negative consequences on their musculoskeletal system and extra-skeletal health. In fact, an optimal vitamin D status is essential to ensure the correct bone, calcium, and phosphate homeostasis. To improve vitamin D status, it is important to not only increase the intake of food fortified with vitamin D, but also to administer vitamin D supplementation when required. Vitamin D3 (cholecalciferol) is the most widely used supplement. In recent years, the administration of calcifediol (25(OH)D3), the direct precursor of the biologically active form of vitamin D3, as oral vitamin D supplementation has progressively grown. Here, we report the potential medical benefits of some peculiar biological actions of calcifediol, discussing the possible specific clinical scenarios in which the oral intake of calcifediol could be most effective to restore the correct serum levels of 25(OH)D3. In summary, the aim of this review is to provide insights into calcifediol-related rapid non-genomic responses and the possible use of this vitamin D metabolite as a supplement for the treatment of people with a higher risk of hypovitaminosis D.
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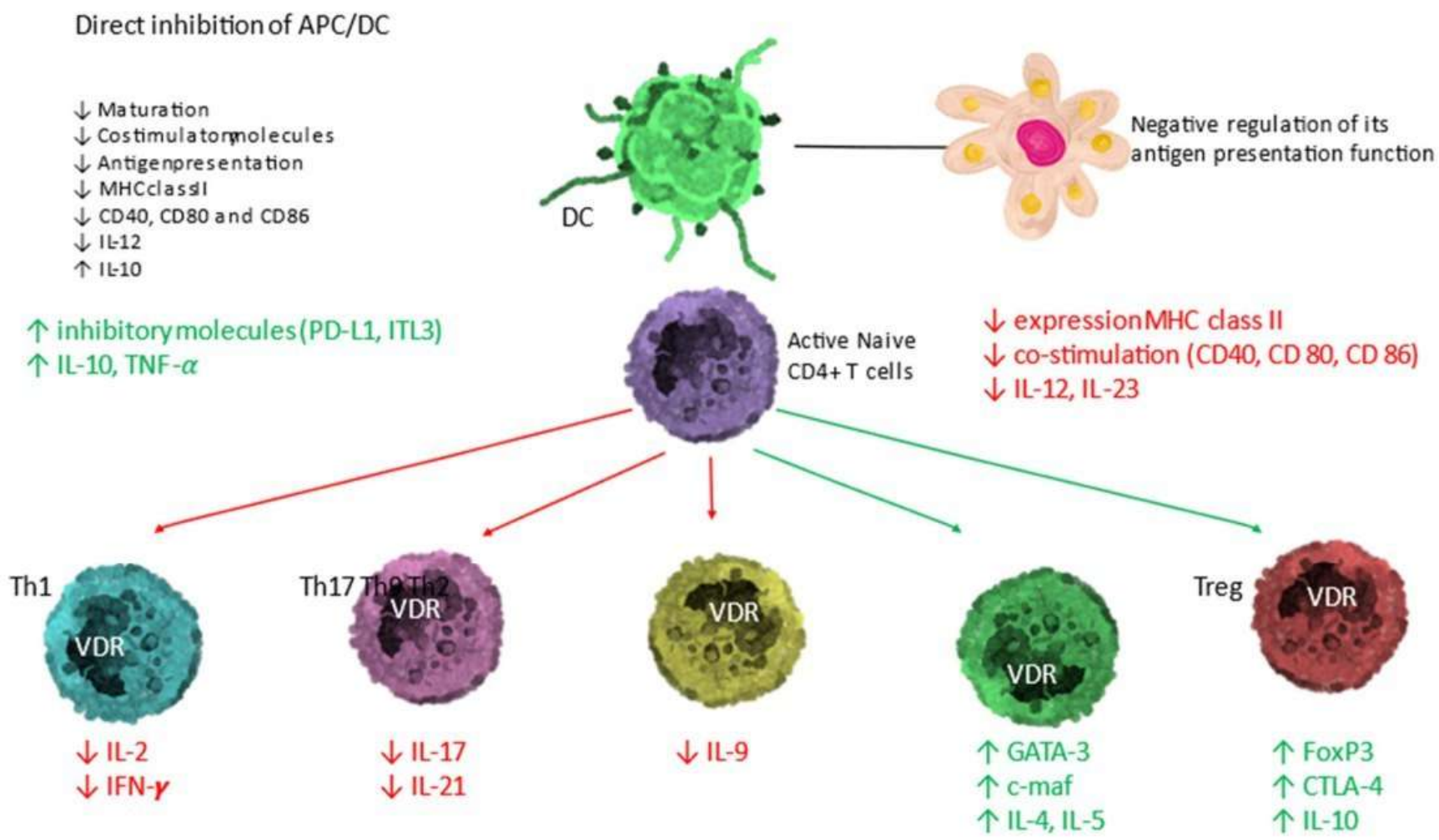
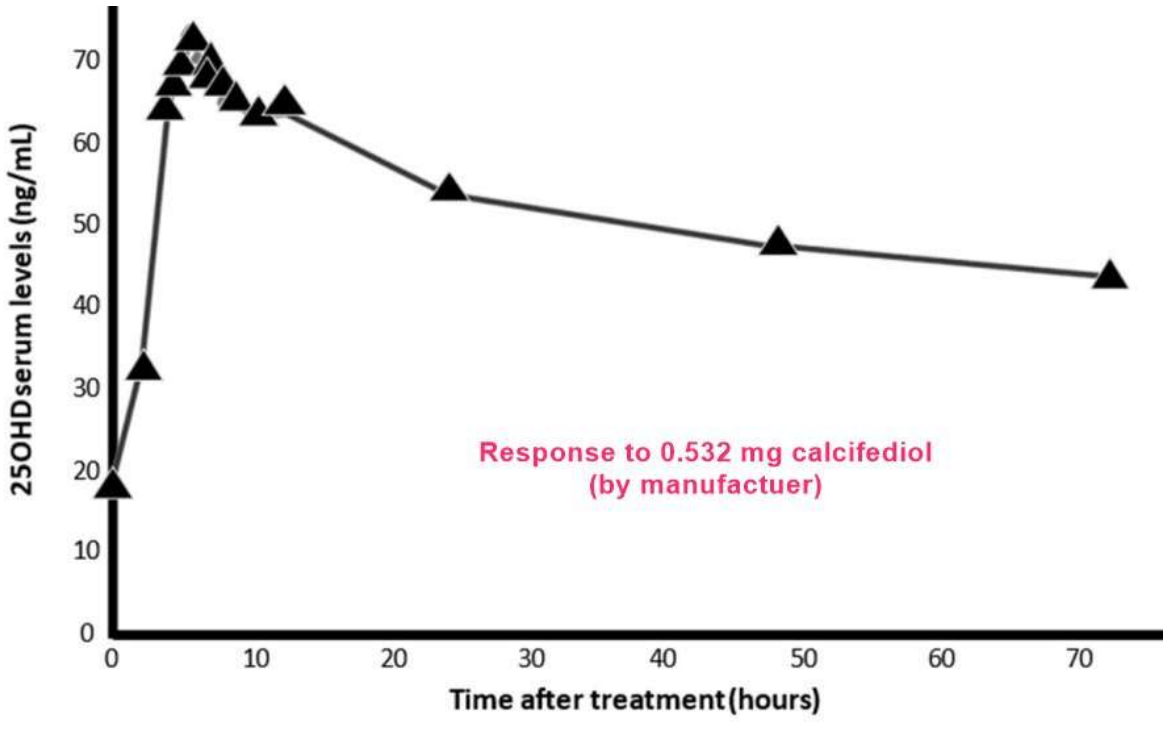
Vitamin D Endocrine System and COVID-19 - Treatment with Calcifediol – June 2022

Nutrients 2022, 14(13), 2716; https://doi.org/10.3390/nu14132716
by Jose Manuel Quesada-Gomez 1,2,*,José Lopez-Miranda 1,3,4ORCID,Marta Entrenas-Castillo 5,Antonio Casado-Díaz 1,2,6ORCID,Xavier Nogues y Solans 2,7ORCID,José Luis Mansur 8ORCID and Roger Bouillon 9,*

The immune system need a good Vitamin D Receptor



Response to Calcifediol



The COVID-19 pandemic is the greatest challenge facing modern medicine and public health systems. The viral evolution of SARS-CoV-2, with the emergence of new variants with in-creased infectious potential, is a cause for concern. In addition, vaccination coverage remains in-sufficient worldwide. Therefore, there is a need to develop new therapeutic options, and/or to optimize the repositioning of drugs approved for other indications for COVID-19. This may include the use of calcifediol, the prohormone of the vitamin D endocrine system (VDES) as it may have potential useful effects for the treatment of COVID-19. We review the aspects associating COVID-19 with VDES and the potential use of calcifediol in COVID-19. VDES/VDR stimulation may enhance innate antiviral effector mechanisms, facilitating the induction of antimicrobial peptides/autophagy, with a critical modulatory role in the subsequent host reactive hyperinflammatory phase during COVID-19: By decreasing the cytokine/chemokine storm, regulating the renin–angiotensin–bradykinin system (RAAS), modulating neutrophil activity and maintaining the integrity of the pulmonary epithelial barrier, stimulating epithelial repair, and directly and indirectly decreasing the increased coagulability and prothrombotic tendency associated with severe COVID-19 and its complications. Available evidence suggests that VDES/VDR stimulation, while maintaining optimal serum 25OHD status, in patients with SARS-CoV-2 infection may significantly reduce the risk of acute respiratory distress syndrome (ARDS) and severe COVID-19, with possible beneficial effects on the need for mechanical ventilation and/or intensive care unit (ICU) admission, as well as deaths in the course of the disease. The pharmacokinetic and functional characteristics of calcifediol give it superiority in rapidly optimizing

25OHD levels in COVID-19. A pilot study and several observational intervention studies using high doses of calcifediol (0.532 mg on day 1 and 0.266 mg on days 3, 7, 14, 21, and 28) dramatically decreased the need for ICU admission and the mortality rate. We, therefore, propose to use calcifediol at the doses described for the rapid correction of 25OHD deficiency in all patients in the early stages of COVID-19, in association, if necessary, with the new oral antiviral agents.

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Calcifediol for Use in Treatment of Respiratory Disease - June 2022

Nutrients 2022, 14(12), 2447; https://doi.org/10.3390/nu14122447

by Marta Entrenas-Castillo 1,2,Lourdes Salinero-González 3,Luis M. Entrenas-Costa 1,2,4 andRubén Andújar-Espinosa 5,6,*

Calcifediol is the prohormone of the vitamin D endocrine system (VDES). It requires hydroxylation to move to 1,25(OH)2D3 or calcitriol, the active form that exerts its functions by activating the vitamin D receptor (VDR) that is expressed in many organs, including the lungs. Due to its rapid oral absorption and because it does not require first hepatic hydroxylation, it is a good option to replace the prevalent deficiency of vitamin D (25 hydroxyvitamin D; 25OHD), to which patients with respiratory pathologies are no strangers. Correcting 25OHD deficiency can decrease the risk of upper respiratory infections and thus improve asthma and COPD control. The same happens with other respiratory pathologies and, in particular, COVID-19. Calcifediol may be a good option for raising 25OHD serum levels quickly because the profile of inflammatory cytokines exhibited by patients with inflammatory respiratory diseases, such as asthma, COPD or COVID-19, can increase the degradation of the active metabolites of the VDES. The aim of this narrative revision is to report the current evidence on the role of calcifediol in main respiratory diseases. In conclusion, good 25OHD status may have beneficial effects on the clinical course of respiratory diseases, including COVID-19. This hypothesis should be confirmed in large, randomized trials. Otherwise, a rapid correction of 25(OH)D deficiency can be useful for patients with respiratory disease.

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Effect of Calcifediol on Physical Performance and Muscle Strength Parameters: A Systematic Review and Meta-Analysis - April 2022

Nutrients 2022, 14(9), 1860; https://doi.org/10.3390/nu14091860

by Mario Barbagallo 1ORCID,Nicola Veronese 1ORCID,Agnese Di Prazza 1ORCID,Francesco Pollicino 1,Luca Carruba 1,Anna La Carrubba 1 andLigia J. Dominguez 1,2,*

1 Geriatric Unit, Department of Internal Medicine and Geriatrics, University of Palermo, 90127 Palermo, Italy

2 Faculty of Medicine and Surgery, Kore University of Enna, 94100 Enna, Italy

There is general agreement that optimal vitamin D status is necessary for bones, muscles, and general health, particularly in older adults, who are at higher risk of negative consequences of vitamin D deficiency, including sarcopenia; vitamin D supplementation is proposed as a potential intervention to mitigate sarcopenia. Several RCTs have reported that calcifediol (25(OH)D) was more potent than cholecalciferol in increasing plasma 25(OH)D. The present systematic review and meta-analysis aimed to summarize the effects of calcifediol on physical performance and muscle strength. We searched databases from inception to 1 January 2022 for studies investigating calcifediol on physical performance or muscle strength parameters. We calculated the difference between the means of follow-up vs. baseline data using standardized mean differences (SMD) and their 95% confidence intervals (CIs); a random-effect model was considered for all of the analyses. Seven RCTs were included in the meta-analysis. Calcifediol significantly improved gait speed (SMD = 2.500; 95%CI = 1.768–3.223; $p < 0.0001$); handgrip strength (n = 5446 participants, SMD = 0.532; 95%CI: 0.305–0.758; $p < 0.0001$; I2 = 20.2%); and leg extension (n = 4318

participants, SMD = 0.641; 95%CI: 0.346 to 0.935; p < 0.0001; I2 = 18.8%;) vs. baseline values. In conclusion, in this systematic review and meta-analysis, we observed that calcifediol may have a positive effect on muscle strength parameters, with less evidence on physical performance. These data further indicate the importance of vitamin D and, in particular, of calcifediol, not only on bone metabolism but also on muscle parameters and sarcopenia.

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See in VitaminDWiki - Muscle strength improved Calfidediol (a form of vitamin D) - meta-analysis May 2022

Treatment of Vitamin D Deficiency with Calcifediol: Efficacy and Safety Profile and Predictability of Efficacy - May 2022

Nutrients 2022, 14(9), 1943; https://doi.org/10.3390/nu14091943

by Jose-Luis Pérez-Castrillon 1,*,Ricardo Usategui-Martín 2,3 andPawel Pludowski 4ORCID

1 Servicio de Medicina Interna, Hospital Universitario Río Hortega, University of Valladolid, 47012 Valladolid, Spain

2 Department of Cell Biology, Histology and Pharmacology, Faculty of Medicine, University of Valladolid, 47003 Valladolid, Spain

3 IOBA, University of Valladolid, 47011 Valladolid, Spain

4 Department of Biochemistry, Radioimmunology and Experimental Medicine, The Children's Memorial Health Institute, 04730 Warsaw, Poland

Table 1. Short-term studies.

Authors	Type of Study	Population	Design	Baseline Vitamin D ng/L/nmol/L	Methods Vitamin D	Superiority of Calcifediol	Other Data
Russo et al. [12]	Open	18 pre- and postmenopausal females	One arm with 500 µg of $25D_3$. 16 weeks	18.1 ± 12.5 ng/mL 45.1 ± 31.1 nmol/L	RIA	NA	88% > 30 ng/mL (74.8 nmol/L)
Minisola et al. [8]	RCT	87 postmenopausal females	Three arms of 25D3 20µg/day, 40 µg/day, 125 µg/week. 16 weeks	16.5 ± 7.5 ng/mL 41.1 ± 18.7 nmol/L	Chemiluminiscence	NA	100% > 30 ng/mL (74.8 nmol/L)
Cashman et al. [13]	RCT	56 adults (25m, 31f) > 50 years	Three arms of 20 µg/day D3, 7 µg/day and 20 µg/day 25D3. 10 weeks	17.4 ± 4.9 ng/mL 43.6 ± 122.3 nmol/L	ELISA	YES	>Dose 20 µg/day 25D3
Bischoff-Ferrari et al. [14]	RCT	20 postmenopausal females	Two arms, 20 µg/day D3 vs. 20 µg/day 25D3. 16 weeks	13 ± 3.8 ng/mL 32.4 ± 9.4 nmol/L	HPLC-MS/MS	YES	-
Jetter et al. [11]	RCT	35 females aged 50–70 years	7 arms: 20 µg/day and 140 µg/week of D3 vs. 20 µg/day and 140 µg/week of 25D3 and combination of both arms. 15 weeks	13 ± 5 ng/mL 32.4 ± 12.4 nmol/L	HPLC-MS/MS	YES	Long-term kinetics similar between the two supplements
Shieh et al. [15]	RCT	35 subjects aged >18 years	Two arms 60 µg/day of D3 vs. 20 µg/day of 25D3. 16 weeks	<20 ng/mL	HPLC-MS/MS	YES	Determination of free vitamin D with superiority of calcifediol
Perez-Castrillón et al. [16]	RCT	303 postmenopausal females	Two arms 625 µg/month D3 vs. 266 µg/month 25D3. 16 weeks	13 ± 3.9 ng/mL 32.4 ± 9.7 nmol/L	Chemiluminiscence	YES	Greater efficacy at one month and four months for both total vitamin D and free vitamin D

RIA: Radioimmunoassay; HPLC: Liquid chromatography; HPLC-MS/MS: Liquid chromatography coupled to tandem mass spectrometry detection.

Table 2. Long-term studies.

Authors	Type of Study	Population	Design	Baseline Vitamin D ng/mL/nmol/L	Methodology Vitamin D	Superiority of Calcifediol	Other Data
Larrosa et al. [18]	Open	70 subjects (11 males and 59 females	After loading dose (1064 µg 25-D3 in 1 month) Three arms: 266 µg /month, 266 µg/3 weeks, 266 µg/2 weeks. 28 ± 14 months	17.6 ± 6 ng/mL 43.9 ± 14.9 nmol/L	RIA	NA	78%, 89%, 93% > 30 ng/mL (74.8 nmol/L) 4%, 11%, 19% > 95 ng/mL (237.1 nmol/L)
Larrosa et al. [19]	Open	129 subjects (109 females, 20 males)	After loading dose (1064 µg 25-D3 in 1 month) Two arms: 20 µg/day D3 vs 266 µg/3 weeks. 12 months	16 ± 5 ng/mL 39.9 ± 12.4 nmol/L	RIA	YES	
Rossini et al. [20]	RCT	271 females	Two arms 21 µg/day D3 vs. 100 µg/week. 12 months	22 ± 6 ng/mL 54.9 ± 14.9 nmol/L	RIA	NO	
Navarro-Valverde et al. [21]	RCT	40 postmenopausal females	4 arms: 20 µg/day D3 vs. 20 µg/day, 266 µg/week, 266 µg/2 weeks 25-D3. 12 months	15.5 ± 1.7 ng/mL 38.7 ± 4.2 nmol/L	HPLC	YES	Dose dependent effect
Ruggero et al. [22]	RCT	67 subjects (42 females and 25 males)	Two arms: 20 µg/day D3 vs. 20 µg/day 25-D3. 7 months	10 (4–16) ng/mL 24.9 (9.9–39.9) nmol/L	RIA	NO	Initial differences but no differences at 210 days
Graeff-Armas et al. [25]	RCT	91 subjects (53 females and 38 males)	Four arms: 20 µg/day D3 vs. 10 µg/day, 15 µg/day, 20 µg/day 25-D3. 6 months	19.2 ± 6.8 ng/mL 48 ± 17 nmol/L	HPLC-MS/MS	YES	Dose dependent effect. Suppression of the supplement reduced vitamin D levels to baseline
Corrado et al. [27]	RCT	160 postmenopausal females	Four arms: 7500 µg single dose, 2500 µg/2 months, 175 µg/week D3 vs. 116 µg/week 25-D3. 6 months	13.4 ± 4.3 ng/mL 33.4 ± 10.7 nmol/L	Chemiluminescence	YES	Dose dependent effect
Jodar E et al. [26]	RCT	303 postmenopausal females	Two arms 625 µg/month D3 vs. 266 µg/month 25D3. 12 months	13 ± 3.9 ng/mL 32.4 ± 9.7 nmol/L	Chemiluminescence	YES	
Gonnelli et al. [28]	RCT	50 osteopenic or osteoporotic females	Two arms, 20 µg/day, 30 µg/day No control with cholecalciferol 6 months	15.6 ± 4.8 ng/mL 39.4 ± 11.9 nmol/L	Chemiluminescence	NA	90 days: 59.3 ng/mL (148 nmol/L) dose 20 µg/day 60 days: 72.3 ng/mL (180.4 nmol/L) dose 30 µg/day

RIA: Radioimmunoassay; HPLC: Liquid chromatography; HPLC-MS/MS: Liquid chromatography coupled to tandem mass spectrometry detection.

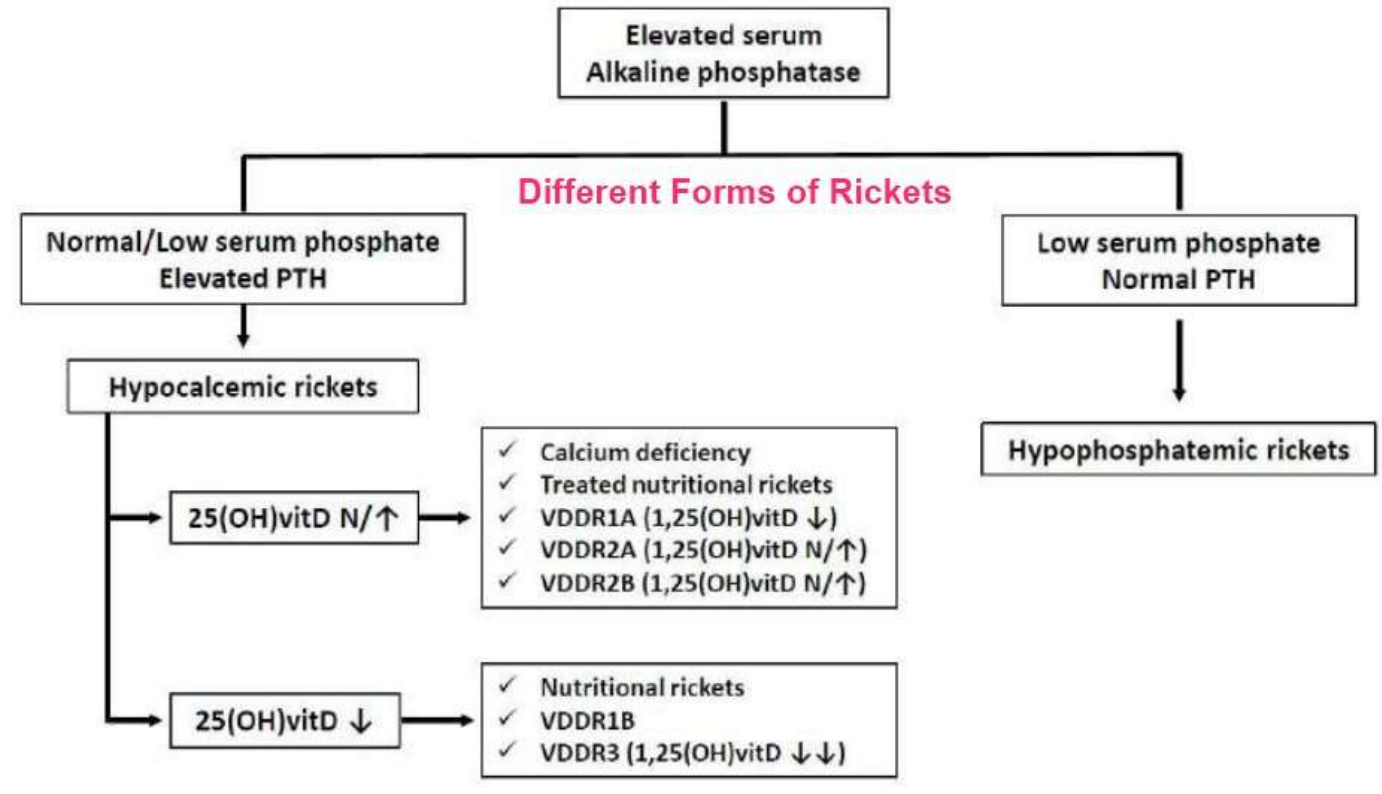
Calcifediol (25-OH-vitamin D3) is the prohormone of the vitamin D endocrine system. It is used to prevent and treat vitamin D deficiency. Calcifediol, as well as cholecalciferol (vitamin D3), is efficient and safe in the general population, although calcifediol has certain advantages over cholecalciferol, such as its rapid onset of action and greater potency. This review analyzed studies comparing the efficacy and safety of both calcifediol and cholecalciferol drugs in the short and long term (>6 months). Calcifediol was found to be more efficacious, with no increase in toxicity. We also assessed the predictability of both molecules. A 25OHD increase depends on the dose and frequency of calcifediol administration. In contrast, after cholecalciferol administration, 25OHD increase depends on more factors than dose and frequency of administration, also phenotypic aspects (such as obesity and malabsorption), and genotypic factors impacts in this increase.

25(OH)Vitamin D Deficiency and Calcifediol Treatment in Pediatrics - April 2022

Nutrients 2022, 14(9), 1854; https://doi.org/10.3390/nu14091854

by Luis Castano *,Leire MadariagaORCID,Gema Grau andAlejandro García-Castaño

Cruces University Hospital, Biocruces Bizkaia Health Research Institute, UPV/EHU, CIBERER/CIBERDEM, Endo-ERN, 48903 Barakaldo, Spain



Vitamin D is essential for the normal mineralization of bones during childhood. Although diet and adequate sun exposure should provide enough of this nutrient, there is a high prevalence of vitamin D deficiency rickets worldwide. Children with certain conditions that lead to decreased vitamin D production and/or absorption are at the greatest risk of nutritional rickets. In addition, several rare genetic alterations are also associated with severe forms of vitamin-D-resistant or -dependent rickets. Although vitamin D3 is the threshold nutrient for the vitamin D endocrine system (VDES), direct measurement of circulating vitamin D3 itself is not a good marker of the nutritional status of the system. Calcifediol (or 25(OH)D) serum levels are used to assess VDES status. While there is no clear consensus among the different scientific associations on calcifediol status, many clinical trials have demonstrated the benefit of ensuring normal 25(OH)D serum levels and calcium intake for the prevention or treatment of nutritional rickets in childhood. Therefore, during the first year of life, infants should receive vitamin D treatment with at least 400 IU/day. In addition, a diet should ensure a normal calcium intake. Healthy lifestyle habits to prevent vitamin D deficiency should be encouraged during childhood. In children who develop clinical signs of rickets, adequate treatment with vitamin D and calcium should be guaranteed. Children with additional risk factors for 25(OH)D deficiency and nutritional rickets should be assessed periodically and treated promptly to prevent further bone damage.

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Calcifediol (25OHD) Deficiency and Its Treatment in Women's Health and Fertility - April 2022

Nutrients 2022, 14(9), 1820; https://doi.org/10.3390/nu14091820

by Ana Arnanz 1,2,Juan A. Garcia-Velasco 1ORCID andJosé Luis Neyro 3,*ORCID

1 IVIRMA, 28023 Madrid, Spain

2 Departamento de Biomedicina y Biotecnología, Universidad de Alcalá de Henares, 28023 Madrid, Spain

3 Academia de Ciencias Médicas de Bilbao, Gynecology and Obstetrics Service, Hospital Universitario Cruces, 48009 Bilbao, Spain

Currently, there is abundant scientific evidence showing that the vitamin D endocrine system (VDES) is a highly complex endocrine system with multiple actions in different regions of the body. The unequivocal presence of vitamin D receptors in different tissues related to fertility, and to specific aspects of women's health such as pregnancy, undoubtedly implies functions of this steroid hormone in both male and female fertility and establishes relationships with different outcomes of human gestation. In order to review the role of the VDES in human fertility, we evaluated the relationships established between 25-hydroxyvitamin D (calcifediol) deficiency and in vitro fertilization, as well as aspects related to ovarian reserve and fertility, and commonly diagnosed endocrinopathies such as polycystic ovary disease. Likewise, we briefly reviewed the relationships between calcifediol deficiency and uterine fibroids, as well as the role that treatment may have in improving human fertility. Finally, the best scientific evidence available on the consequences of calcifediol deficiency during pregnancy is reviewed in

relation to those aspects that have accumulated the most scientific literature to date, such as the relationship with the weight of the newborn at the time of delivery, the appearance of preeclampsia, and the risk of developing gestational diabetes and its final consequences for the pregnancy. To date, there is no definitive consensus on the necessary dose for treatment of calcifediol deficiency in the therapeutic management of infertility or during pregnancy. Large prospective clinical intervention studies are needed to clarify the benefits associated with this supplementation and the optimal dose to use in each situation. Although most intervention studies to date have been conducted with cholecalciferol, due to its much longer history of use in daily care, the use of calcifediol to alleviate 25-hydroxyvitamin D deficiency seems safe, even during pregnancy. The unequivocal presence of vitamin D receptors in very different tissues related to human fertility, both male and female, as well as in structures typical of pregnancy, allows us to investigate the crucial role that this steroid hormone has in specific aspects of women's health, such as pregnancy and the ability to conceive. Well-designed clinical studies are needed to elucidate the necessary dose and the best form of treatment to resolve the very common calcifediol deficiency in women of reproductive age

Calcifediol (25OH Vitamin D3) Deficiency: A Risk Factor from Early to Old Age - March 2022

Nutrients 2022, 14(6), 1168; https://doi.org/10.3390/nu14061168

by Roger Bouillon 1,*,Leen Antonio 1,2ORCID andOscar Rosero Olarte 3ORCID

1 Clinical and Experimental Endocrinology, Department of Chronic Diseases and Metabolism, Catholic University of Leuven, 3000 Leuven, Belgium

2 Department of Endocrinology, University Hospitals Leuven, 3000 Leuven, Belgium

3 Clinical Endocrinology, Asociación Colombiana de Osteoporosis, Bogotá 500005, Colombia

Vitamin D deficiency is the main cause of nutritional rickets in children and osteomalacia in adults. There is consensus that nutritional access to vitamin D can be estimated by measuring serum concentrations of 25OHD and vitamin D deficiency can thus be considered as calcifediol deficiency. However, the threshold for vitamin D/calcifediol sufficiency remains a matter of debate. Vitamin D/calcifediol deficiency has been associated with musculoskeletal effects but also multiple adverse extra-skeletal consequences. If these consequences improve or if they can be treated with vitamin D supplementation is still unclear. Observational studies suggest a higher infection risk in people with low calcifediol levels. There is also a consistent association between serum calcifediol and cardiovascular events and deaths, but large-scale, long-term intervention studies did not show any benefit on cardiovascular outcomes from supplementation, at least not in subjects without clear vitamin D deficiency. Cancer risk also did not change with vitamin D treatment, although there are some data that higher serum calcifediol is associated with longer survival in cancer patients. In pregnant women, vitamin D supplementation decreases the risk of pre-eclampsia, gestational diabetes mellitus, and low birth weight. Although preclinical studies showed that the vitamin D endocrine system plays a role in certain neural cells as well as brain structure and function, there is no evidence to support a beneficial effect of vitamin D in neurodegenerative diseases. Vitamin D supplementation may marginally affect overall mortality risk especially in elderly subjects with low serum calcifediol concentrations.

Rapid Nontranscriptional Effects of Calcifediol and Calcitriol - March 2022

Nutrients 2022, 14(6), 1291; https://doi.org/10.3390/nu14061291

by Simone Donati 1,Gaia Palmini 1ORCID,Cinzia Aurilia 1,Irene Falsetti 1,Francesca Miglietta 1,Teresa Iantomasi 1ORCID andMaria Luisa Brandi 2,*

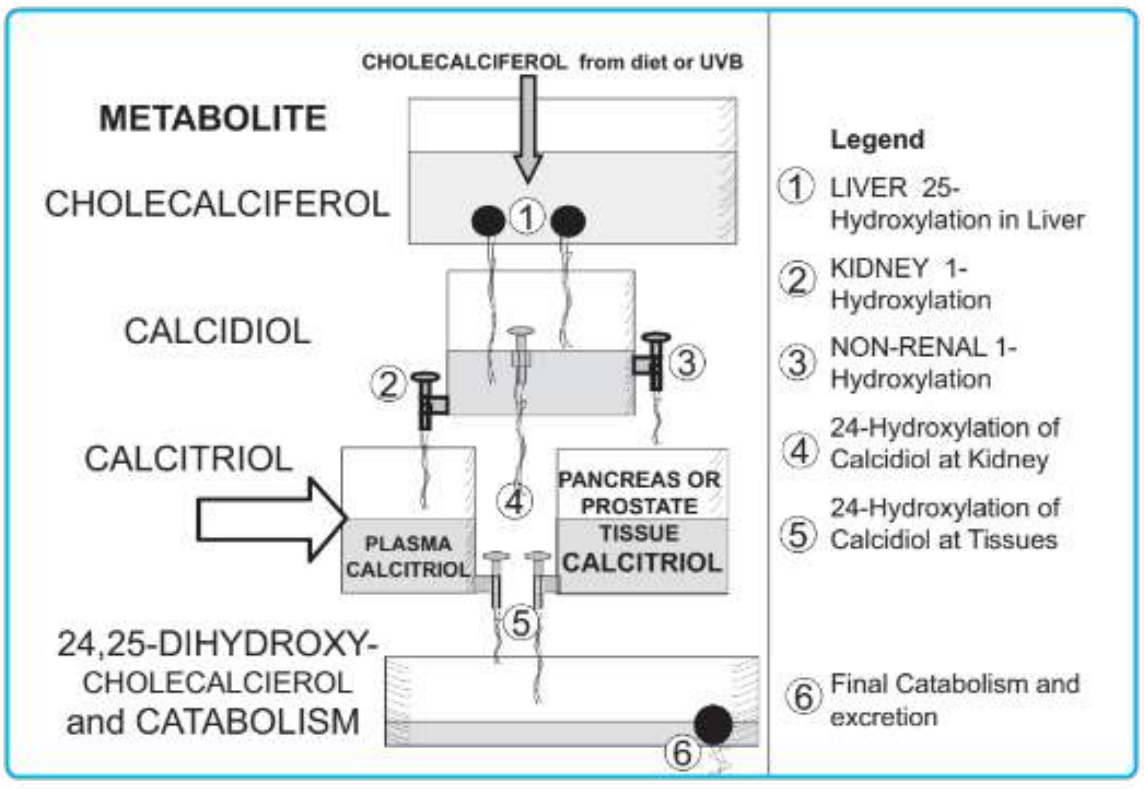
1 Department of Experimental and Clinical Biomedical Sciences, University of Florence, 50139 Florence, Italy
2 Fondazione Italiana Ricerca sulle Malattie dell'Osso (F.I.R.M.O. Onlus) Italian Foundation for the Research on Bone Diseases, 50141 Florence, Italy

Classically, a secosteroid hormone, vitamin D, has been implicated in calcium and phosphate homeostasis and has been associated with the pathogenesis of rickets and osteomalacia in patients with severe nutritional vitamin D deficiency. The spectrum of known vitamin D-mediated effects has been expanded in recent years. However, the mechanisms of how exactly this hormone elicits its biological function are still not fully understood. The interaction of this metabolite with the vitamin D receptor (VDR) and, subsequently, with the vitamin D-responsive element in the region of specific target genes leading to the transcription of genes whose protein products are involved in the traditional function of calcitriol (known as genomic actions). Moreover, in addition to these transcription-dependent mechanisms, it has been recognized that the biologically active form of vitamin D3, as well as its immediate precursor metabolite, calcifediol, initiate rapid, non-genomic actions through the membrane receptors that are bound as described for other steroid hormones. So far, among the best candidates responsible for mediating rapid membrane response to vitamin D metabolites are membrane-associated VDR (VDRm) and protein disulfide isomerase family A member 3 (Pdia3). The purpose of this paper is to provide an overview of the rapid, non-genomic effects of calcifediol and calcitriol, whose elucidation could improve the understanding of the vitamin D3 endocrine system. This will contribute to a better recognition of the physiological acute functions of vitamin D3, and it could lead to the identification of novel therapeutic targets able to modulate these actions.

Vitamin D supplementation: cholecalciferol, calcifediol, and calcitriol - Vieth 2020

Eur J Clin Nutr. 2020 Nov;74(11):1493-1497. doi: 10.1038/s41430-020-0697-1 PDF is behind a paywall

Reinhold Vieth 1



The specific compound that is meant for use in the context of vitamin D supplementation is often ambiguous. The term "supplementation" has been used in the context of cholecalciferol, ergocalciferol, calcidiol, and calcitriol. In nature, by far the major form of vitamin D that nurtures the body is cholecalciferol. In contrast, ergocalciferol is primarily a synthetic and less stable product which is less potent per microgram dose than is cholecalciferol. Calcidol is the major circulating metabolite of cholecalciferol, while calcitriol is the hormone that upregulates the active transport of calcium from the gut, and which suppresses parathyroid hormone secretion. Nutrition policy papers and guidelines leave unstated the obvious fact that calcidiol and calcitriol are not nutrients, and that those metabolites are not pertinent to food fortification or dietary supplementation.

Recent evidence shows that ergocalciferol is not stable with storage, and it is far more susceptible to breakdown with cooking and baking than is cholecalciferol. Therefore, it must be concluded that cholecalciferol is the only form of vitamin D that should be considered in the context of the nutritional functions of fortification and supplementation.

VitaminDWiki VIRUS pages with CALCIDIOL etc. in title (7 as of May 2023)

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Items found: 7

Title	Modified
Calcifediol (semi-activated Vitamin D) might treat Respiratory Diseases such as COVID - July 2022	19 Jul, 2022
Large dose of calcifediol or vitamin D up to 15 days before COVID hospitalization reduced death rates (1.5X, 1.3X) – Dec 2021	04 Dec, 2021
7X less likely to go to ICU if COVID-19 ward gave calcifediol (semi-activated Vitamin D) – July 2021	07 Jul, 2021
5X less likely to enter ICU with COVID-19 if get Calcifediol (semi-activated vitamin D) - RCT Feb 19, 2021	13 Feb, 2021
MATH plus protocol for COVID-19 includes Calcifediol or Vitamin D - Jan 2021	26 Jan, 2021
COVID-19 defeated by calcifediol form of Vitamin D in Spain - pilot RCT Aug 29, 2020	22 Nov, 2020
Hepatitis C drug is extremely expensive, why not try Calcidiol (semi-processed vitamin D) - May 2014	07 May, 2014

41+ VitaminDWiki pages have CALCIDIOL etc. in title

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Title	Modified
Vitamin D supplementation vs Calcifediol	19 Jan, 2024
Calcifediol (semi-activated vitamin D, generally by prescription) – Oct 2023	20 Oct, 2023
Fast responses to Vitamin D – loading dose, nanoemulsion and Calcifediol – April 2023	15 Apr, 2023
Vitamin D genes may be more important than (25(OH)D) to orthopedics – Review Dec 2022	08 Dec, 2022
Responses to 3600 IU Vitamin D or Calcifediol – Oct 2022	04 Oct, 2022
Calcidiol quickly raises vitamin D level in pigs, but does not appear to provide any benefits – Aug 2022	01 Sep, 2022
Calcidiol (bacterial fermentation-derived vitamin D) OK with pigs (perhaps lower cost) - Aug 2022	13 Aug, 2022
Calcifediol (semi-activated Vitamin D) might treat Respiratory Diseases such as COVID - July 2022	19 Jul, 2022
Calcifediol (Calcidiol, semiactivated Vitamin D) - many studies	29 Jun, 2022

Title	Modified
Calcidiol	17 May, 2022
COVID test positive 2X less likely if high vitamin D, Calcifediol looking good, etc. – Dec 31, 2021	01 Jan, 2022
Large dose of calcifediol or vitamin D up to 15 days before COVID hospitalization reduced death rates (1.5X, 1.3X) – Dec 2021	04 Dec, 2021
Calcifediol (Calcidiol) is far less cost-effective and available than Vitamin D – RCT June 2021	04 Sep, 2021
Calcidiol (Calcifediol, ampli-D) approved as food supplement by EFSA – (10 micrograms per day) – July 2021	13 Jul, 2021
7X less likely to go to ICU if COVID-19 ward gave calcifediol (semi-activated Vitamin D) – July 2021	07 Jul, 2021
Calcidiol increased blood levels of Vitamin D in one month (dogs) – Feb 2021	10 Jun, 2021
Calcifediol is superior to cholecalciferol (it mainly acts faster) – RCT June 2021	10 Jun, 2021
Cows gave more milk after pregancy if given Calcidiol (semi-activated Vitamin D) – RCT March 2021	05 Mar, 2021
5X less likely to enter ICU with COVID-19 if get Calcifediol (semi-activated vitamin D) - RCT Feb 19, 2021	13 Feb, 2021
Response to weekly Calcifediol in 4 months - RCT Aug 2022	03 Feb, 2021
Is HyD (25(OH)D) a better form of vitamin D for some animals and maybe humans with liver problems	03 Feb, 2021
MATH plus protocol for COVID-19 includes Calcifediol or Vitamin D - Jan 2021	26 Jan, 2021
COVID-19 defeated by calcifediol form of Vitamin D in Spain - pilot RCT Aug 29, 2020	22 Nov, 2020
Calcifediol (Calcidiol) might be a better form of Vitamin D for some people – May 2019	09 May, 2019
Calcifediol (25(OH)D3) may be 4 X better than Vitamin D for fortification – Aug 2018	29 Jan, 2019
Oral calcidiol is a good form of vitamin D supplementation – Aug 2017	22 Dec, 2017
Poorly functioning livers do not process vitamin D (Calcidiol is needed) – Sept 2014	27 May, 2017
Calcidiol may be 5X more effective than Vitamin D3 – June 2012	25 Jan, 2017
Vitamin D3 becomes Calcidiol which becomes Calcitriol	25 Jan, 2017
25-Hydroxyvitamin D3 suppresses hepatitis C virus production – Oct 2012	17 May, 2016
Pigs have about 2X less variation in response to calcidiol as humans do to vitamin D – 2015	06 Dec, 2015
Nano-encapsulated of Vitamin D3, Calcidiol, calcitriol look promising, esp time release – Dec 2012	03 Oct, 2015
Vitamin D and calcidiol are not hormones, but calcitriol is a hormone – Aug 2014	26 Jul, 2015
Vitamin D can be converted into calcifediol by microbes – May 2015	23 May, 2015

Title	Modified
Modified release active Vitamin D (calcifediol) for those with poor Kidney function (USD 10,000 per year) – April 2015	16 Apr, 2015
VITAMINA D Y CÁNCER: ACCIÓN ANTINEOPLÁSICA DE LA 1α,25(OH)2 -VITAMINA D3	14 Nov, 2014
Patent for combination of vitamin D3 and calcifediol– Sept 2009	10 Sep, 2014
Hepatitis C drug is extremely expensive, why not try Calcidiol (semi-processed vitamin D) - May 2014	07 May, 2014
25(OH)D (Calcidiol) in animal-based food adds about 80 IU of equivalent daily vitamin D – March 2014	18 Mar, 2014
After bone fracture, vitamin D unchanged but 1,25(OH)(2) D decreased – Jan 2013	05 Jan, 2014
130% more piglets after giving gilt Calcidiol, a form of vitamin D – Nov 2012	20 Aug, 2013
How much calcidiol or calcitriol is needed to slow aging in mice – 2009	02 Jul, 2010

Short url = is.gd/calcifediol

The original document is available at https://vitamindwiki.com/Calcifediol+%28Calcidiol%2C+semiactivated+Vitamin+D%29+-+many+studies