Vitamin D Metabolism/Mechanism

The biochemical physiology of vitamin D metabolism is one of the more complicated and detailed pathways to be familiar with. Incorporating multiple pathways, organs and the use of sunlight to arrive at the metabolically active form of vitamin D, calcitriol, this mechanism can be understood by viewing the reactions and sites involved more closely.

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Mechanism Of Action

Ergocalciferol (Vitamin D2)
Eagle-casserole
This is a consumable form of vitamin D that is found in plants or used as a dietary supplement. After absorption in the intestines, ergocalciferol undergoes conversion to 25-hydroxyvitamin D2 in the liver.

Plant Sources
Plants
Natural sources of vitamin D are quite rare outside of fish liver and plants. Ergocalciferol, or vitamin D2, is plant-based and aids in securing adequate levels of active vitamin D precursors.

Cholecalciferol (Vitamin D3)
Coal-casserole
7-dehydrocholesterol undergoes conversion to cholecalciferol. There is a small amount that becomes 25-hydroxyvitamin D2, but this form has less affinity for vitamin D-binding protein and a shorter half-life, making it a suboptimal form.

Sunlight Conversion in Skin
Sunlight on Skin
UV B light exposure from direct sunlight on the skin results in conversion of 7-dehydrocholesterol to previtamin D3 briefly, followed by temperature-induced rearrangement to cholecalciferol, a form of vitamin D3. Following this conversion, cholecalciferol traverses the bloodstream to the liver for further changes.

7-Dehydrocholesterol
Lucky (7) Slot-machine with Daisy-cholesterol-burgers
Found primarily within the epidermis of the skin, 7-dehydrocholesterol is an endogenous precursor to vitamin D3 that employs UV sunlight for conversion to cholecalciferol.

Liver Hydroxylation
Liver
Whether originating from intestinal absorption or conversion from epidermal UV exposure, cholecalciferol arrives at the liver for hepatic hydroxylation. This results in the conversion of cholecalciferol to 25-hydroxyvitamin D3, or calcifediol. Ergocalciferol is hydroxylated to 25-hydroxyvitamin D2 but this is less clinically significant.

25-(OH) D (25-hydroxyvitamin D)
(25) Quarter (OH)-(D) Daisy
Upon arrival to the liver as cholecalciferol after conversion from 7-dehydrocholesterol, an enzyme called 25-hydroxylase catalyzes the conversion to 25-hydroxyvitamin D (sometimes written as 25-hydroxyvitamin D3 or 25-(OH) D3), also known as calcifediol.

Storage Form

Storage-purse

The status of vitamin D levels in the body is measured by lab studies testing for 25-hydroxyvitamin D3, as this is the stored form of the vitamin. 25-(OH) D3 is not significantly influenced by parathyroid hormone (PTH), giving it an advantage over the active form of vitamin D, calcitriol.

Kidney Hydroxylation

Kidney

After conversion to 25-hydroxyvitamin D3 (calcifediol) in the liver, these molecules progress to the proximal tubules of the kidneys, where they again undergo hydroxylation. This occurs using the enzyme 1-alpha-hydroxylase to become 1,25 dihydroxyvitamin D, or calcitriol, which is the active metabolite of vitamin D.

1,25-(OH)2 D (1,25-dihydroxyvitamin D)

(1) Wand, (25) Quarter-(OH) (2) Tutu

The final hydroxylation of cholecalciferol to calcitriol in the kidneys marks the formation of active vitamin D. Upon release from the tubular cells in the kidney, this form of vitamin D is able to affect significant physiologic change in the calcium, phosphorus and PTH pathways.

Active Form Calcitriol

Active Calcified-troll

The final, active installment of vitamin D is called 1,25 dihydroxyvitamin D, or calcitriol. Despite this being the active form, testing for its levels has no diagnostic value. This is due to the influence of PTH on its serum values.

Absorbs Calcium and Phosphorus in Intestine

Absorbs Calcium-cow and Phosphorus-P in Intestine

There are many physiologic roles of this now active vitamin D metabolite, called calcitriol. These include (1) increasing intestinal absorption of calcium and phosphorus, (2) diminishing calcium excreted by the kidneys, and (3) activating osteoblasts to aid calcification of bone. The activity of calcitriol is related to feedback loops with PTH and calcium. Low serum calcium causes the parathyroid gland to release PTH, which acts to promote renal conversion of calcifediol to calcitriol, which in turn increases calcium levels.