



University of Fallujah  
College of Medicine



## Vitamin D

**Lecture : 4**

**Stage : 2<sup>nd</sup> Stage**

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**Department: Chemistry and Biochemistry**

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# Learning Objectives

- Understand what is vit D?
- Understand the structures and metabolism of vitamin D.
- Identify the clinical roles of vitamin D deficiency

**Vitamin D** is a group of fat-soluble secosteroids responsible for intestinal absorption of **calcium and phosphate**.

It is not actually an essential dietary vitamin, as it can be synthesized in adequate amounts by most mammals exposed to sunlight.

**Calcitriol**: is the physiological active form of vitamin D, it increases the blood calcium level.

**Calcitonin**: is the peptide hormone released from thyroid gland, it decreases the blood calcium.

**Calcitonin, calcitriol & PTH act together**

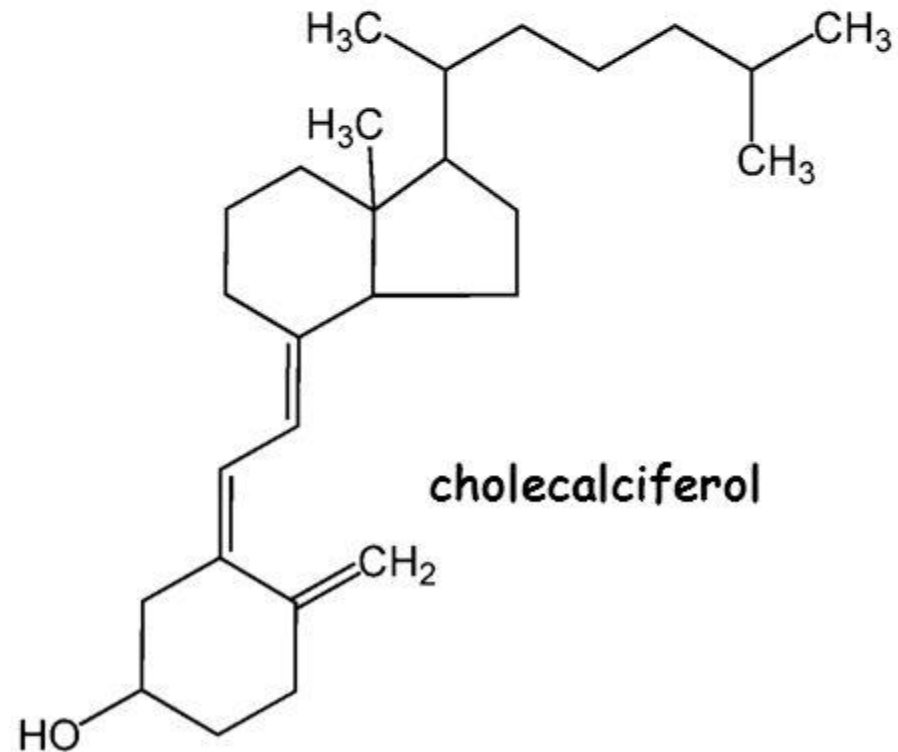
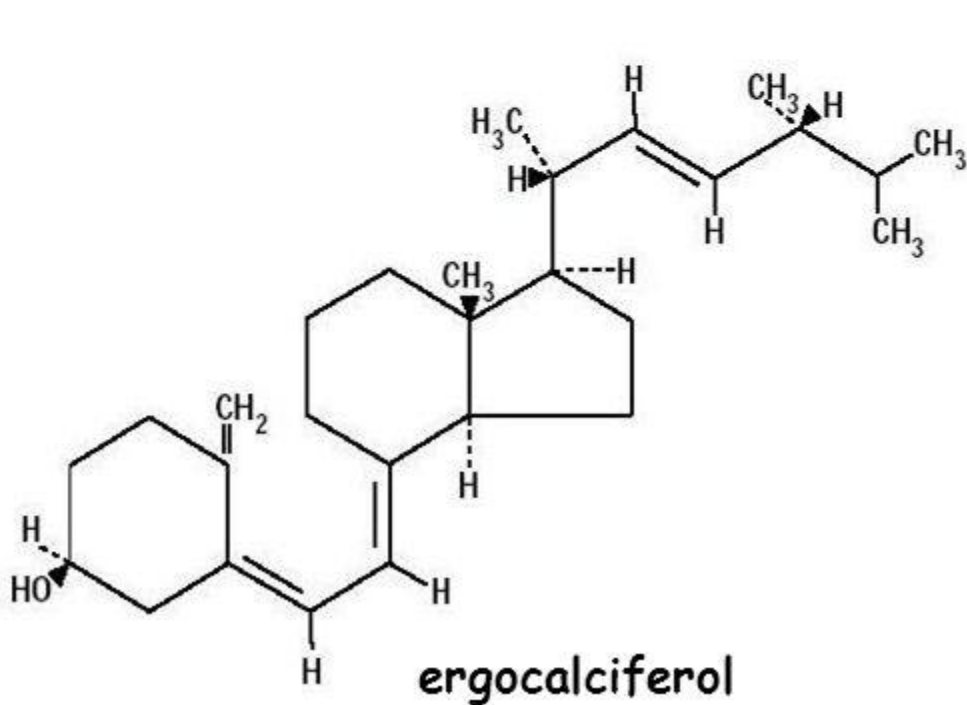


Vitamin D is also known as calciferol, comprises a group of fat-soluble seco-sterols. The two major forms are vitamin **D<sub>2</sub>** and vitamin **D<sub>3</sub>**.

Vitamin D<sub>2</sub> (**ergocalciferol**) is largely human-made and added to foods, whereas vitamin D<sub>3</sub> (**cholecalciferol**) is synthesized in the skin of humans from 7-dehydrocholesterol and is also consumed in the diet via the intake of animal-based foods.

# Two forms of vitamin D

- Vitamin D2 - ergocalciferol
- Vitamin D3 - cholecalciferol



## Table 1. Forms of Vitamin D

### **Cholecalciferol (vitamin D<sub>3</sub>)**

Naturally occurring form of vitamin D; made by the skin upon sun exposure; found in foods and most supplements

### **Calcidiol (25-hydroxyvitamin D<sub>3</sub>)**

Prehormone made directly from cholecalciferol in the liver; low biologic activity, but major form circulating in the bloodstream; concentrations measured by typical blood test for vitamin D deficiency

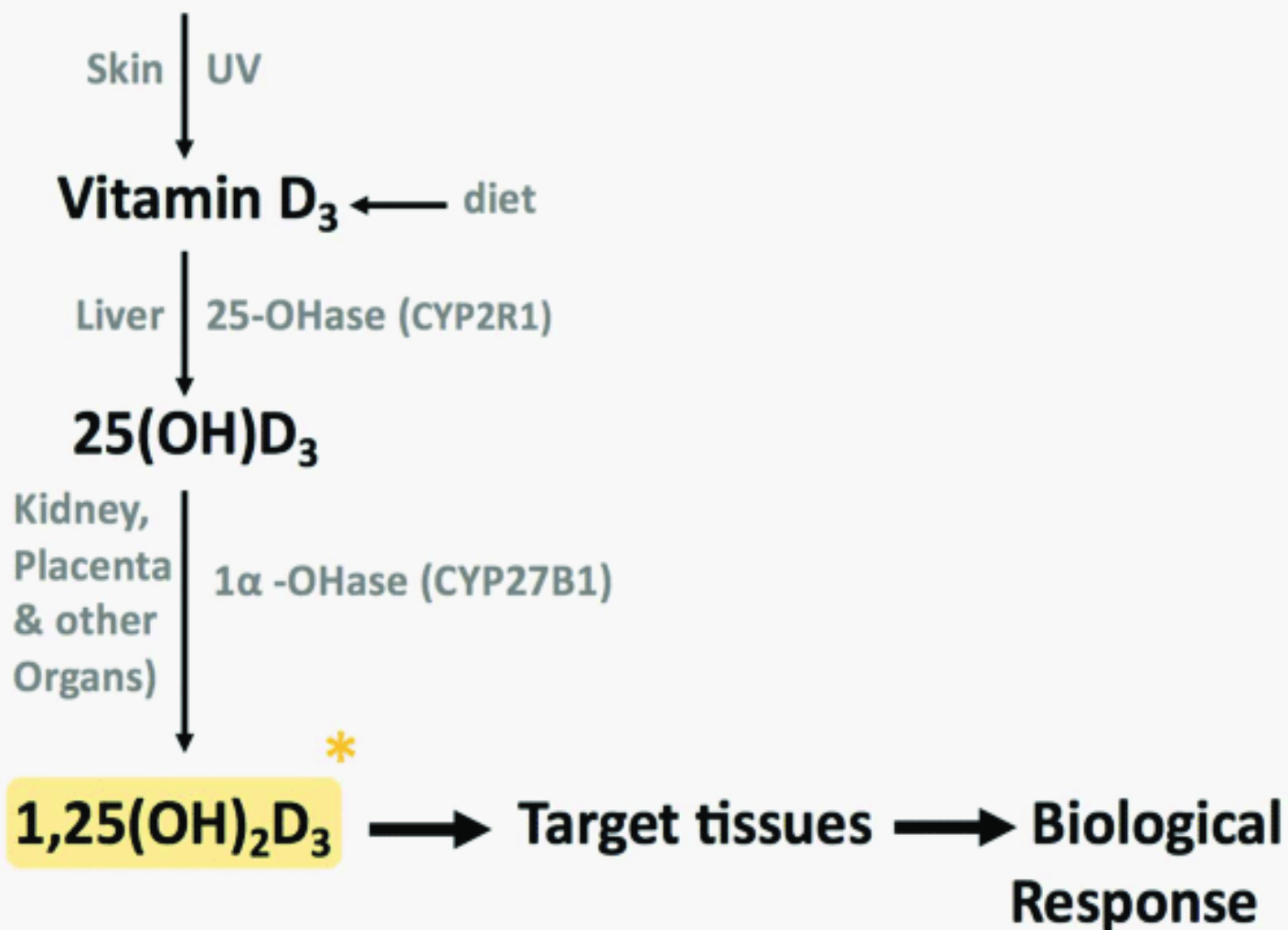
### **Calcitriol (1,25-dihydroxyvitamin D<sub>3</sub>)**

Activated form made from calcidiol in the kidneys and tissues; the most potent steroid hormone in the body

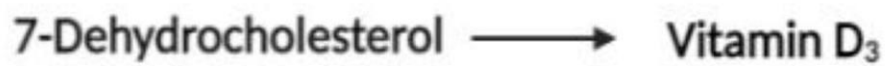
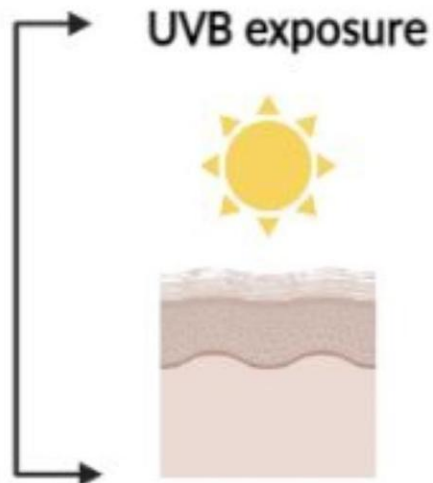
### **Ergocalciferol (vitamin D<sub>2</sub>)**

Made in the laboratory by radiating fungus; not naturally occurring in the body; used in prescription vitamin D (Drisdol), available in 50,000-IU capsules

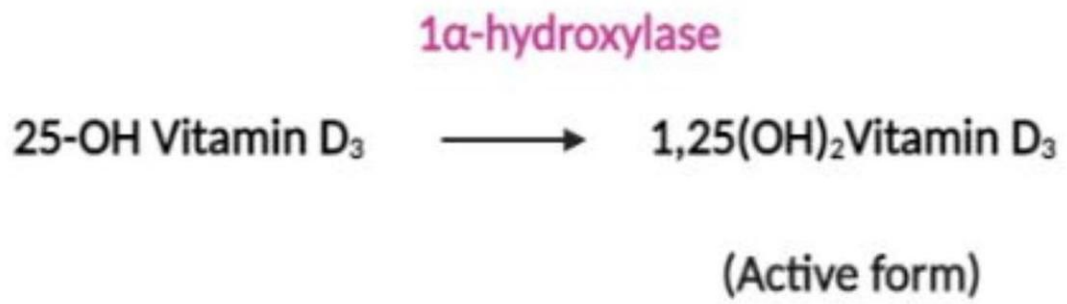
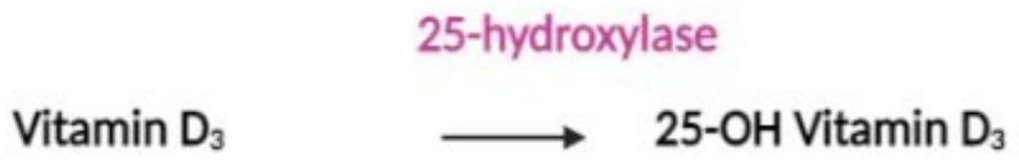
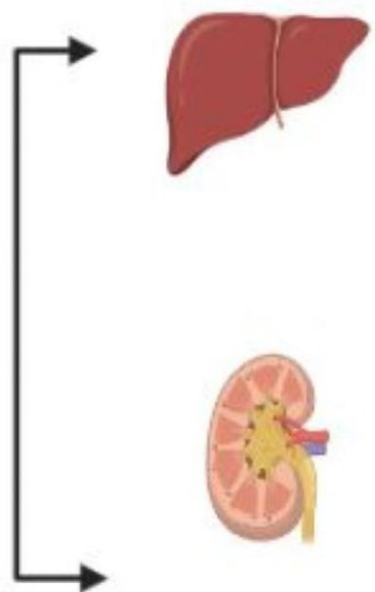
## 7-dehydrocholesterol



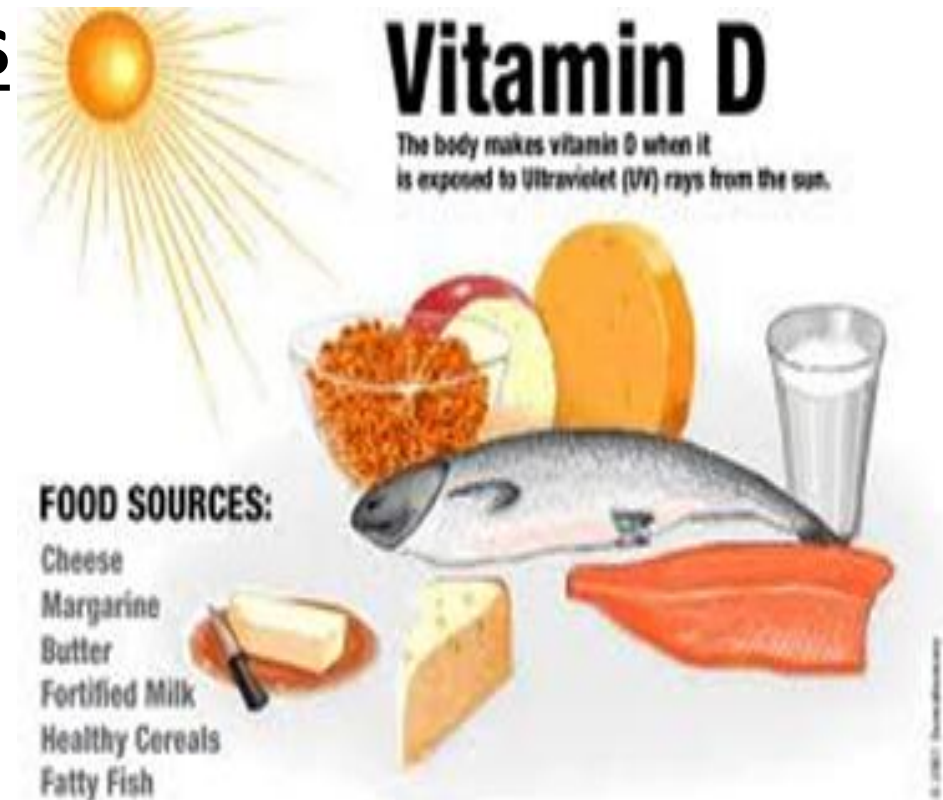
## Vitamin D<sub>3</sub> Synthesis



## Vitamin D<sub>3</sub> Activation



- Sources of Vitamin D
- 1- Food
- 2- Sun exposure
- 3-Dietary supplements



## • METABOLISM

- Vitamin **D3** produced in the epidermis must be further metabolized to **be active**.
- The **first step, 25-hydroxylation**, takes place primarily in the liver, although other tissues have this enzymatic activity as well. There are several 25-hydroxylases.
- **25OHD** is the major **circulating form** of vitamin D. However, in order for vitamin D metabolites to achieve **maximum biologic activity they must be further hydroxylated in the 1 $\alpha$  position** by the enzyme CYP27B1;
- **1,25(OH)2D** is the **most potent metabolite** of vitamin D and accounts for most of its **biologic actions**.

- The activity of the 1,  $\alpha$ - hydroxylase depends on:
- **a-Parathyroid hormone and plasma calcium:** a low level of plasma calcium stimulates 1, $\alpha$ -hydroxylase through the secretion of parathyroid hormone.
- **b-Plasma Phosphate:** reduced plasma phosphate activates the 1, $\alpha$ - hydroxylase but independent of parathyroid hormone.
- **c-Insulin,growth hormone prolactin and estrogen** are affect (increase) the production of active form of vitamin D.

- Hepatic production of 25OHD.
- The next step in the bioactivation of **D2 and D3**, is the hydroxylation to **25OHD**. **25OHD** is the major circulating form of vitamin D and provides a clinically useful marker for vitamin D status.
- Renal production of 1, 25(OH) 2D.
- 1,25(OH)2D is the **most potent metabolite** of vitamin D, and mediates most of its hormonal actions especially those involving the **vitamin D receptor (VDR)**, 1,25(OH)2D is produced from 25OHD by the enzyme **25OHD-1 $\alpha$ hydroxylase (CYP27B1)**.
- Renal production of 24, 25(OH) 2D. The kidney is also the major producer of a second important **metabolite of 25OHD**, namely **24, 25(OH) 2D**, and the enzyme responsible is **25OHD-24 hydroxylase**.

# Calcium balance

Maintenance of serum calcium concentrations within a narrow range is vital for normal functioning of the nervous system, as well as for bone growth and maintenance of bone density. Vitamin D is essential for the efficient utilization of calcium by the body

The parathyroid glands sense serum calcium concentrations and secrete parathyroid hormone (PTH) if calcium concentrations decrease below normal .

Elevations in PTH stimulate the activity of the **25-hydroxyvitamin D<sub>3</sub>-1 $\alpha$ -hydroxylase enzyme in the kidney**, resulting in the **increased** production of **1 $\alpha$ ,25-dihydroxyvitamin D**, after releasing the active form into the circulation and transported to target tissues.

Within target cells, 1 $\alpha$ ,25-dihydroxyvitamin D binds to and induces the **activation of VDR**, which leads to changes in gene expression that normalize serum calcium by :

**(1)** increasing the intestinal absorption of dietary calcium, **(2)** increasing the reabsorption of calcium filtered by the kidneys, and **(3)** mobilizing calcium from bone when there is insufficient dietary calcium to maintain normal serum calcium concentrations .



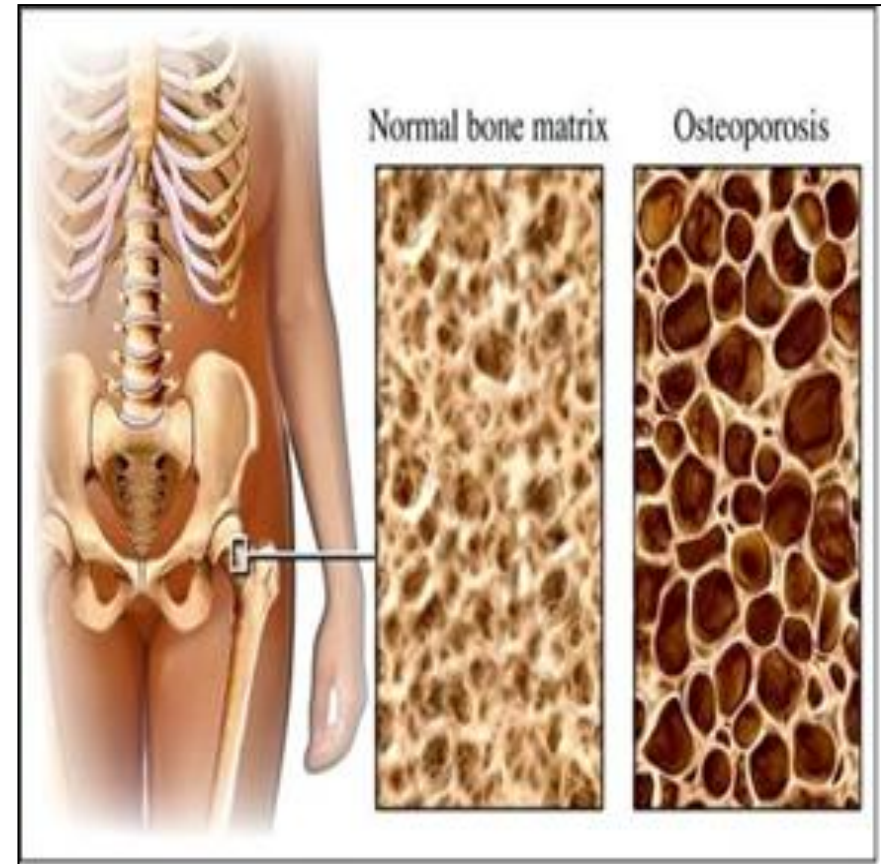
- **Vitamin D Deficiency**

- **Vitamin D deficiency is known to cause several bone diseases including:**
- **1-Rickets**, a childhood disease characterized by impeded growth, and deformity, of the **long bones**.
- **2-Osteomalacia**, a bone-thinning disorder that occurs exclusively in adults and is characterized by **proximal** muscle weakness and bone fragility.
- **3-Osteoporosis**, a condition characterized by reduced **bone mineral density** and increased bone fragility.
- **4-Muscle aches and weakness.**
- **5-Muscle twitching .**

**In general,** the two main causes of vitamin D deficiency are:

**1-** Not getting enough vitamin D in your diet and/or through sunlight.

**2-** The body isn't properly absorbing or using vitamin D.



- Vitamin D deficiency can occur for a number of reasons:

**1-Don't consume the recommended levels of the vitamin over time.**

**2-Breastfed infants •**

**3-Older adults •**

**4-Exposure to sunlight is limited.**

**5-Have dark skin.**

**6- People with fat malabsorption (Digestive tract cannot adequately absorb vitamin D).**

**7- Kidneys cannot convert vitamin D to its active form.**