Q.11

Vitamin D is a generic term and indicates a molecule of the general structure shown for rings A, B, C and D with different side chain structures.

- The A, B, C & D ring structure is derived from the cyclopentanoperhydrophenanthrene ring structure for steroids.
- Technically, vitamin D is classified as a seco-steroid.

- Seco steroids → are those in which one of the rings have been broken; in vitamin D, the 9,10 carbon-carbon bond of ring B is broken.

- Vitamin D2 = ergocalciferol (found in plant)
  - completely synthetic form produced by the irradiation of the plant steroid ergosterol.
- Vitamin D3 = cholecalciferol (found in animal tissue).
  - produced photochemically by the action of sunlight or ultraviolet light from the precursor of sterol 7-dehydrocholesterol
  - Vitamin D = Calciferol.

Endogenous vitamin D precursor:

Pro vitamin D.

- 7-dehydrocholesterol:

an intermediate in cholesterol synthesis, is converted to cholecalciferol in the dermis and epidermis of humans exposed to sunlight.

Sources:

- Good source → Exposure to sunlight.
  Fish, egg yolk, fish liver oil.

- Moderate amount → milk.

RDA

10 ug.
10 ug.
5 ug
20 ug

- children : 10 ug/day
- Pregnancy : 10 ug/day
  Lactation
- adults : 5 ug/day.
- above 60 years : 20 ug/day.

- Metabolism of vitamin D.

formation of Calcitriol.

- Humans and animals can produce vitamin D inside their bodies from cholesterol.
- cholesterol is converted to 7-dehydro. cholesterol (7DC) which is a precursor of vitamin D_3.
- Exposure to the UV rays in sunlight convert 7DC → cholecalciferol.

{ vitamin D_2 & D_3 - are not Biologically active}

- Converted in vivo to active form {calcitriol}.
- Includes two hydroxylation reactions
- one in liver & another in kidney.

- cholecalciferol —25-hydroxylase (LIVER)→ 25-Hydroxy cholecalciferol

1,25-hydroxylase or 1-α hydroxylase. (KIDNEY)

1,25 - dihydroxy cholecalciferol {calcitriol} CALCITRIOL

- 1,25 - DHC acts as a hormone rather than a vitamin
- Hepatic 25 - hydroxylase → microsomal. mono oxygenase Required CYT-P450 and NADPH.

25-HCC.

- 25-HCC → Major storage form of vitamin D.

- 25-HCC Bounds to VDBP (vitamin D binding protein, an α - 2 globulin).

- 1α hydroxylase → located in mitochondria of PCT. requires cytochrome P450, NADPH. and ferrodoxin (Fe-S protein)

- calcitriol ⟹ active form of vitamin D.

3 sites of action.

- Intestinal villi cell
- Bone
-

Intestine

- promotes the absorption of Ca and P from the intestine.
- 1,25-$(OH)_2$ D binds to vitamin D receptor (VDR) in nucleus
- Induces the synthesis of calbindin {Ca-binding protein}

Bone -

Increases activity of osteoblast → ↑ mineralization of Bone.

- Osteoblast secrete alkaline phosphatase.
- hydrolyses phosphate ester bonds
- releases phosphorous.

Kidney

- increases reabsorption of Ca and P by renal tubules.

OTHER FUNCTIONS OF CALCITRIOL

- Immune system: important for cell mediated immunity & coordination of immune response.
- cell differentiation.

- reduce risk of cancer and coronary vascular diseases.

Vitamin D.

- Increase calcium release from bone.
- Increases calcium absorption from

Regulation of calcitriol

Factors regulating calcitriol production

→ Ca, P, PTH.

→ feed back control.

Parathyroid hormone (PTH)

- calcium sensor protein in the thyroid gland
  - detects low plasma calcium concentration.
- Effects of parathyroid hormone.

→ stimulates 1α-hydroxylase activity in kidneys

$$25\text{-OH D} \longrightarrow 1,25\text{-}(OH)_2\text{D}.$$

Summary of calcitriol regulation.

plasma Ca ↓

↓

PTH ↑

↓

Calcitriol ↑

↓

Ca mobilisation from bone ↑

renal reabsorption of ca

↓

Renal excretion of Ca. ↓

↓

Ca absorption from intestine ↑

↓

plasma Ca ↑

plasma Ca level increased

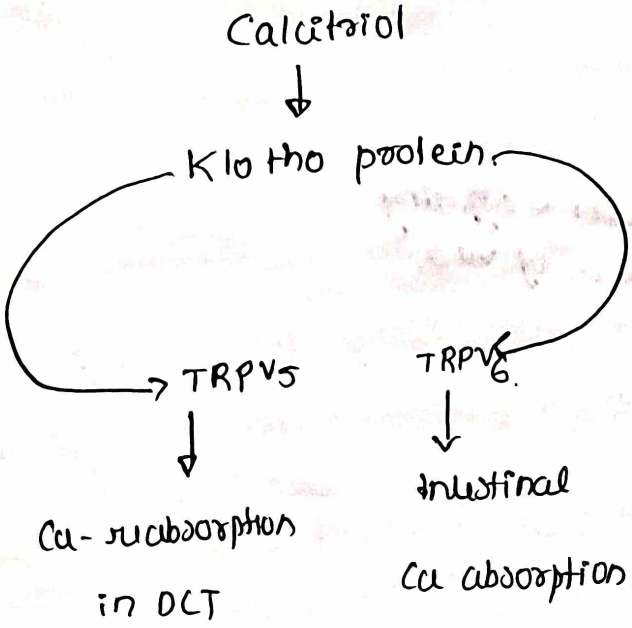
↑ Ca level / Adequate Vit D

↓

Hydroxylation at 24th position (kidney)

↓

formation of 24, 25 DHCC is less active.



Serum vitamin D_3

- reference levels of serum 25(OH) D_3 is 30 ng/ml (75nmol/L)
- level less than 10 ng/ml is the mark of severe vitamin D deficiency.

vitamin D deficiency. → Anti Rachitic vitamin.

- Rickets in children
- osteomalacia. in adults.

(1) Lack of sunshine.

(2) dietary deficiency of vit D.

Breast milk 0 - 10 IU/100 ml
cows milk. 0.3 - 4 IU/100ml
Egg yolk 25 IU / average yolk.

(3) Improper Ca & P ratio

(4) diseases and drug:

liver disease, renal disease - affecting activation of vit D.

(•) Gastrointestinal diseases.

(•) Antiepileptic

(•) Glucocorticosteroid.

(5) defective absorption of vitamin D -

- obstructive jaundice
- steatorrhea
- High phytate content in diet.