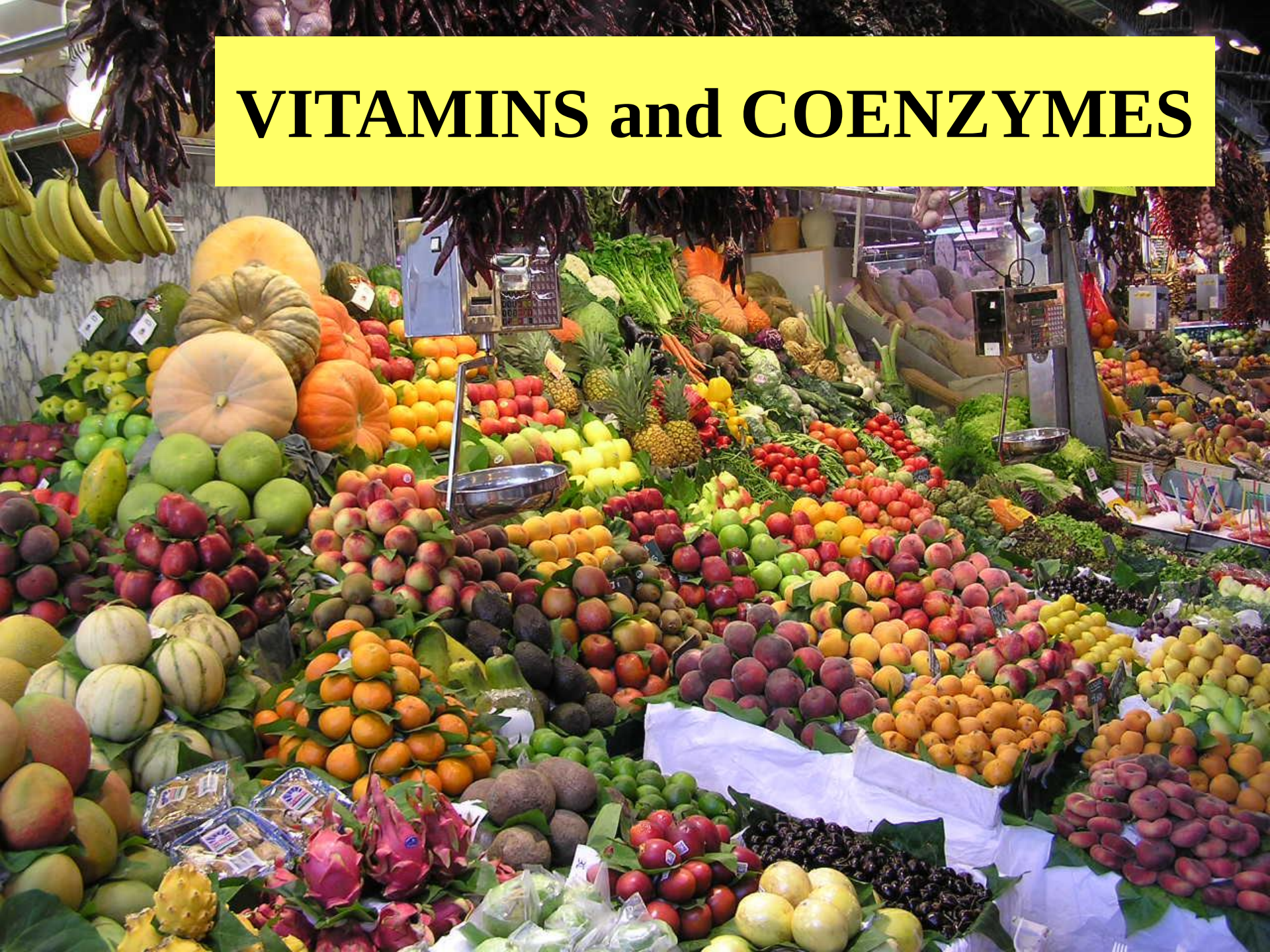
VITAMINS and COENZYMES



Introduction to Vitamins

VITAL + AMINES = VITAMIN

- **Organic** molecules, essential for the normal growth and development, required in tiny amounts

- Cannot be synthesized by mammalian cells must be supplied in the diet

  Vitamin C –vitamin for human
  Vitamin K, H – synthesized by gut flora
  Vitamin A - from precursor beta carotene

FUNCTIONS

- Regulate metabolism, help convert lipids and saccharides into energy (B-complex)
- Hormones (vitamin D)
- Antioxidants (vitamin E, C, beta carotene)
- Regulators of cell and tissue growth and differentiation (vitamin A)
- Coenzyme precursors (B-complex)

AVITAMINOSIS - chronic or long-term vitamin lack (beri-beri, scurvy, rickets and pellagra)

HYPOVITAMINOSIS - any of several diseases caused by deficiency of one or more vitamins

HYPERVITAMINOSIS – the condition resulting from the chronic excessive intake of vitamins (vitamin supplements) side effects – nausea, diarrhea, vomiting

Avitaminoses

Vitamin deficiency causes:

Vitamin A - xerophthalmia night blindness

Thiamine (B_1) - beri-beri

Niacin (B_3) - pellagra

Vitamin B_{12} - megaloblastic anemia

Vitamin C - scurvy

Vitamin D - rickets, osteomalacia

Vitamin K - impaired coagulation

- Rare in developed world - fortification

ANTIVITAMINS

- **substances that destroy or inhibit the metabolic action of a vitamin**

Antivitamins - chemotherapy of several infectious diseases

Classification:

1. Enzymes decomposing vitamins (tiaminase, ascorbase)
2. Compounds forming nonactive complexes with vitamins (avidin)
3. Compounds structurally similar to vitamins (sulphonamides)

Water Soluble Vitamins	Fat Soluble Vitamins
Thiamine (B1)	Vitamin A - Retinol
Riboflavin (B2)	Vitamin D - Calciferol
Niacin (B3)	Vitamin E - Tocoferol
Pantothenic acid (B5)	Vitamin K – Quinons
Pyridoxin (B6)	Vitamin F – essential fatty acids
Biotin (B7) – vitamin H	
Folic acid (B9)	
Cobalamin (B12)	
Ascorbic acid (vit. C)	

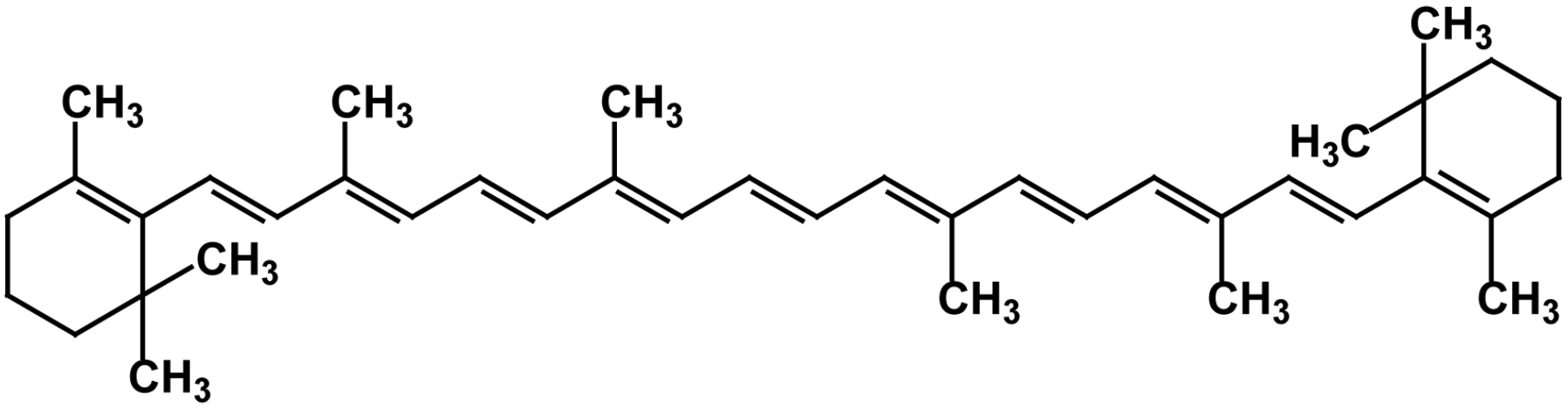
VITAMIN A (R E T I N O L)

Its provitamin - β-carotene - (red, orange pigments in plants and fruits)

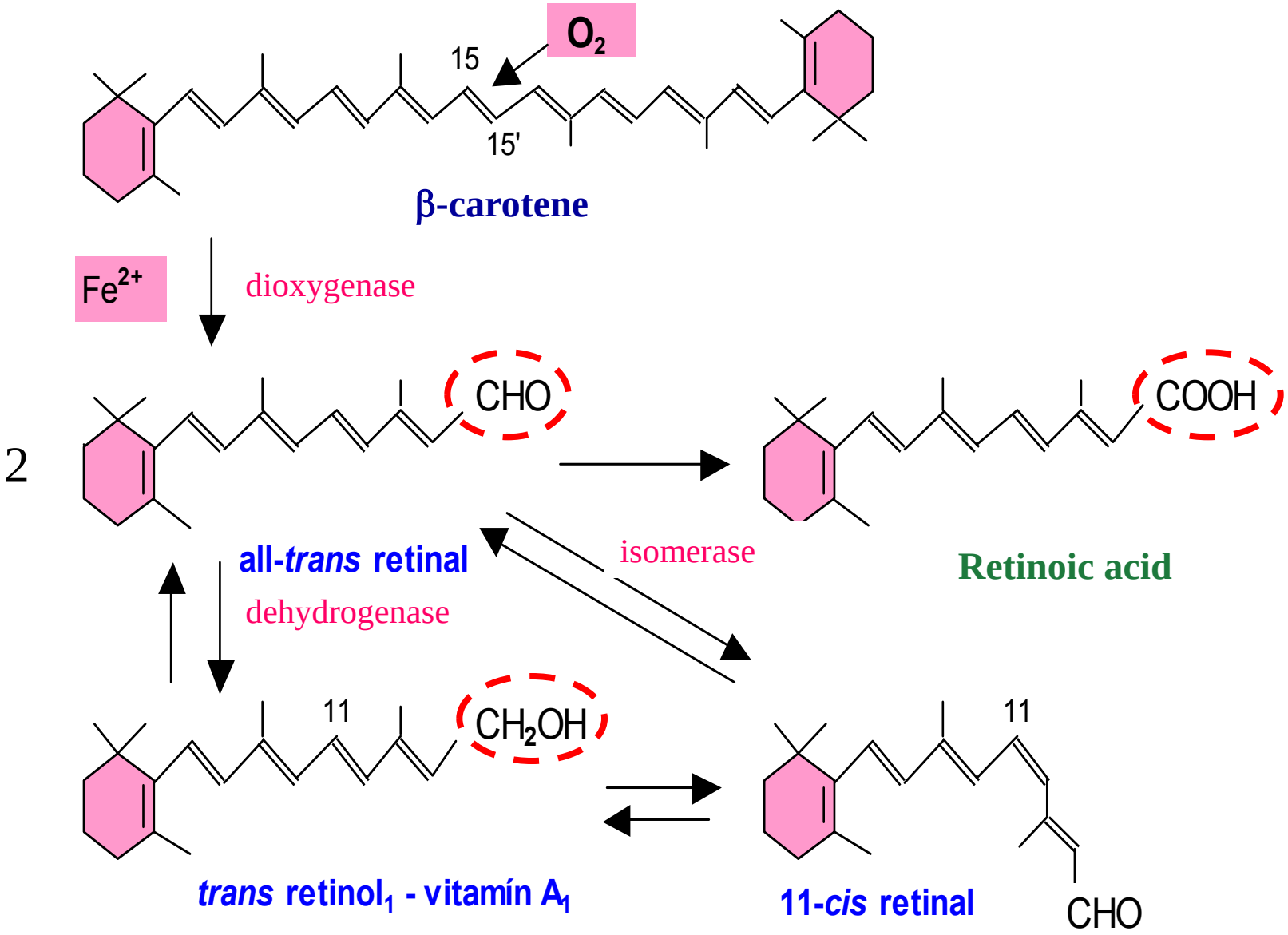
- Antioxidant

Structure: tetraterpenoid containing β-ionone ring with an unsaturated side chain

α-, β- a γ- provitamin A



β-CAROTENE


O2
15
15'
β-carotene
Fe2+
dioxygenase
2
CHO
COOH
all-trans retinal
isomerase
Retinoic acid
dehydrogenase
11
CH2OH
11
trans retinol1 - vitamín A1
11-cis retinal
CHO

Functions of vitamin A

Vision – retinal is a structural part of **rhodopsin** (visual purple) – light sensitive pigment in retina

- **Bone** remodeling – function of osteoblasts and osteoclasts depend on it.

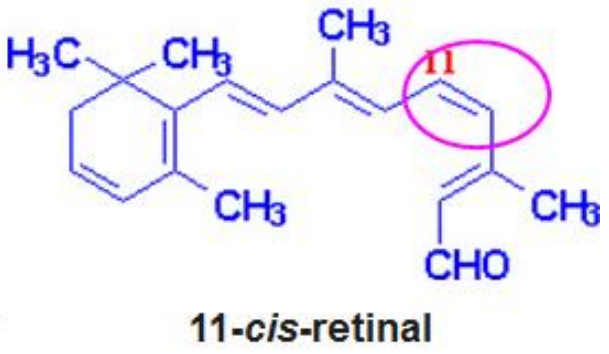
- **Reproduction** – sperm production, menstrual period

VISION CYCLE

RETINA

RHODOPSIN
(PIGMENT)

LIGHT



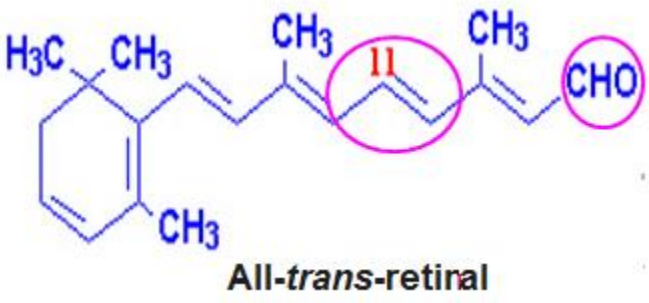
11-*cis*-retinal

cis-RETINAL ⟵ **OPSIN** ⟶ **trans-RETINAL-OPSIN**

NERVE IMPULS

RETINAL ISOMERASE

TRANS-RETINAL



All-*trans*-retinal

DEHYDROGENASE

$NADH+H^+$

NAD^+

TRANS -RETINOL

Retinolesters (liver)
transport by blood proteins

HYPOVITAMINOSIS A

- **Night blindness –** mild deficiency of vitamin A – inability to produce sufficient amount of rhodopsin (lack of retinal)

- Large deficiency of vit. A – **xeroftalmia** – keratinisation of the eye tissue (today in Africa, Asia)

VITAMINS D - CALCIFEROL

- **Increases Ca in the bloodstream** by promoting absorption of Ca and P from food in the intestines and reabsorption of Ca in the kidneys, **enabling normal mineralization of bones**

2 major forms:

D_2 – derived from precursor **ergosterol** present in plants

D_3 – derived from precursor **7-dehydrocholesterol** present in skin

Structure similar to steroid hormones - derived from cholesterol

UV

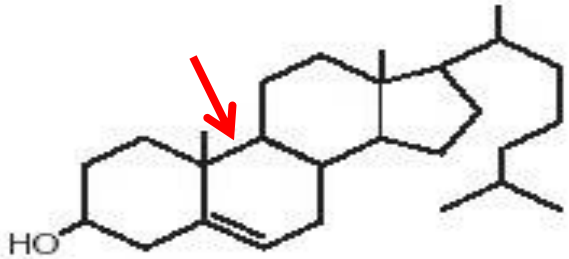
7-dehydrocholesterol (skin) → **cholecalciferol**
(provitamin) **(D_3, calciol)**

UV

Ergosterol (plants) → **ergocalciferol (D_2, ercalciol)**

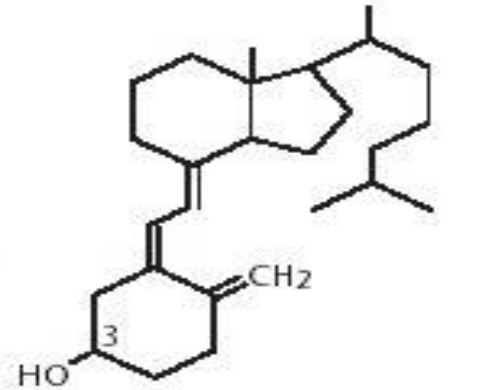
(provitamin)

Adequate amounts of vitamin D_3 can be made in the skin after only **10 -15 minutes** of sun exposure at least 2x per week to the face, arms, hands, or back without sunscreen



7-Dehydrocholesterol

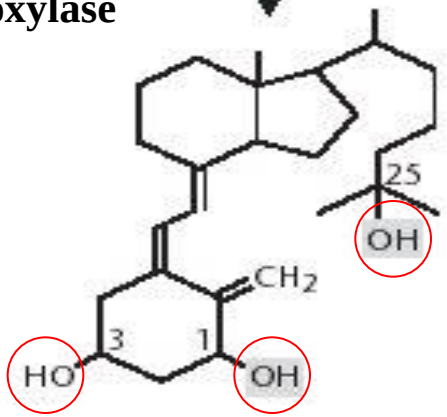
UV



Cholecalciferol (Calciol)
= Provitamin D

Kidneys: 25-hydroxylase

Liver: 1-hydroxylase



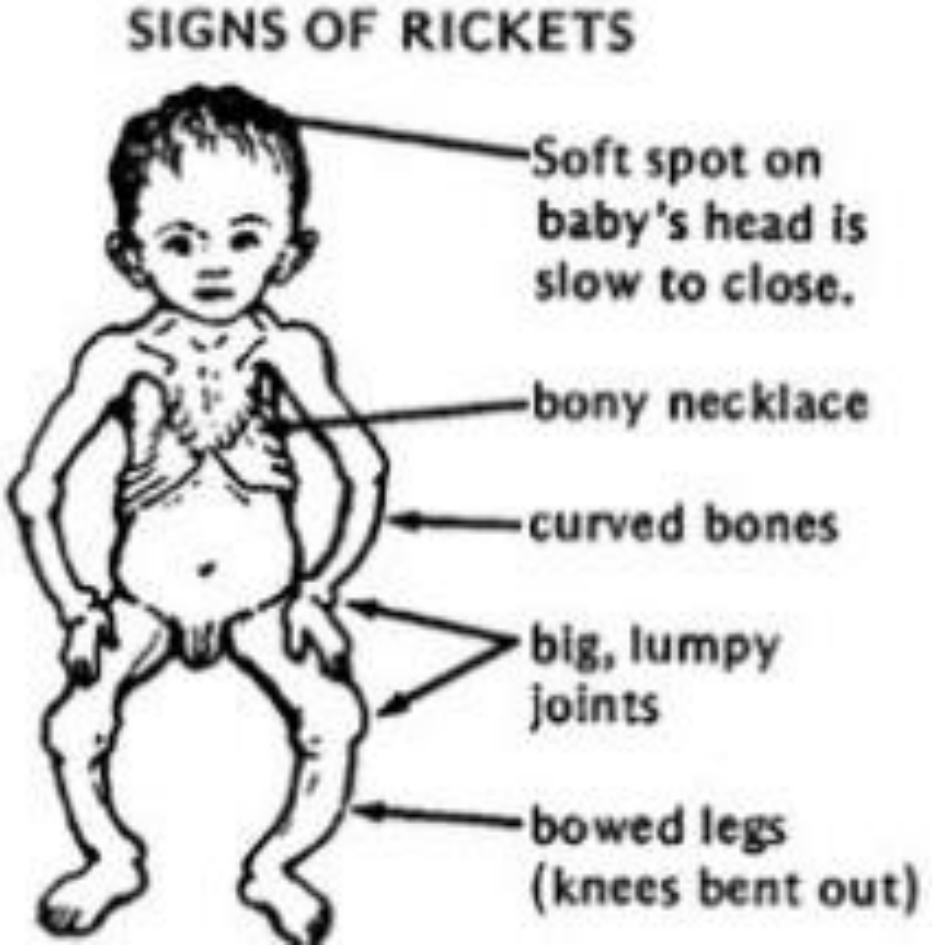
1,25-Dihydroxycholecalciferol (Calcitriol)
= „D-Hormon"

DEFICIENCY

Leads to impaired bone mineralization, and to bone softening diseases including:

- **RICKETS** - a childhood disease - impeded growth, and deformity of the long bones

- **OSTEOMALACIA** - softening of the bones caused by impaired bone metabolism primarily due to inadequate levels of available phosphate, calcium, and vitamin D

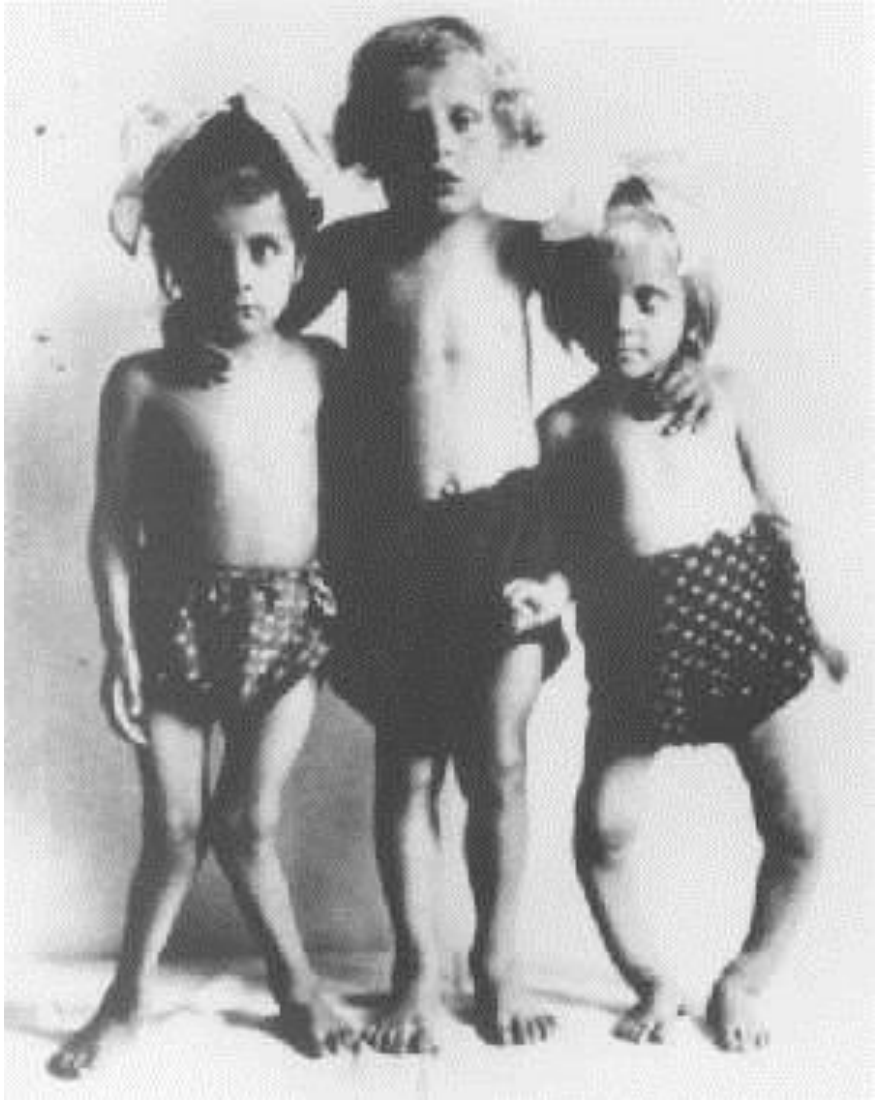


ve to spine or

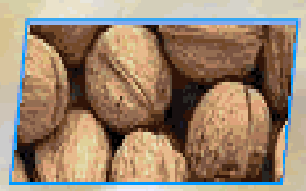
Wide joints elbow and wrist

Odd-shaped legs

Osteomalacia



Vitamin E – Tocopherols
antisterile vitamin



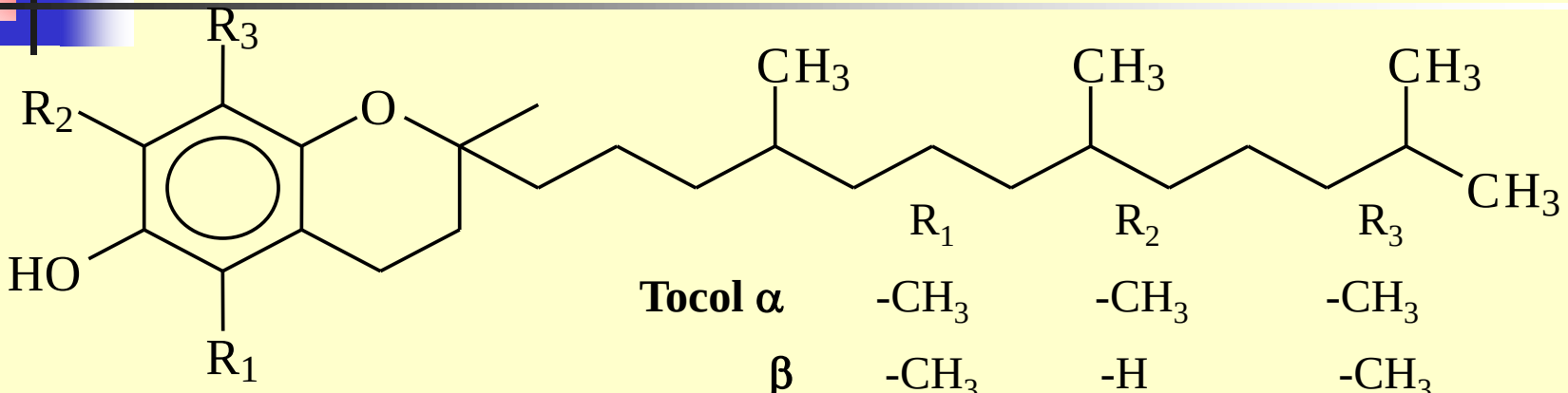
Benefits

- Protects lipids (cell membranes), DNA, proteins from oxidation – **ANTIOXIDANT**

  Protects food fats from going rancid
- Helps to form red blood cells

STRUCTURE: tocol, forms 8 basic derivatives

α-tocopherol is the most effective form

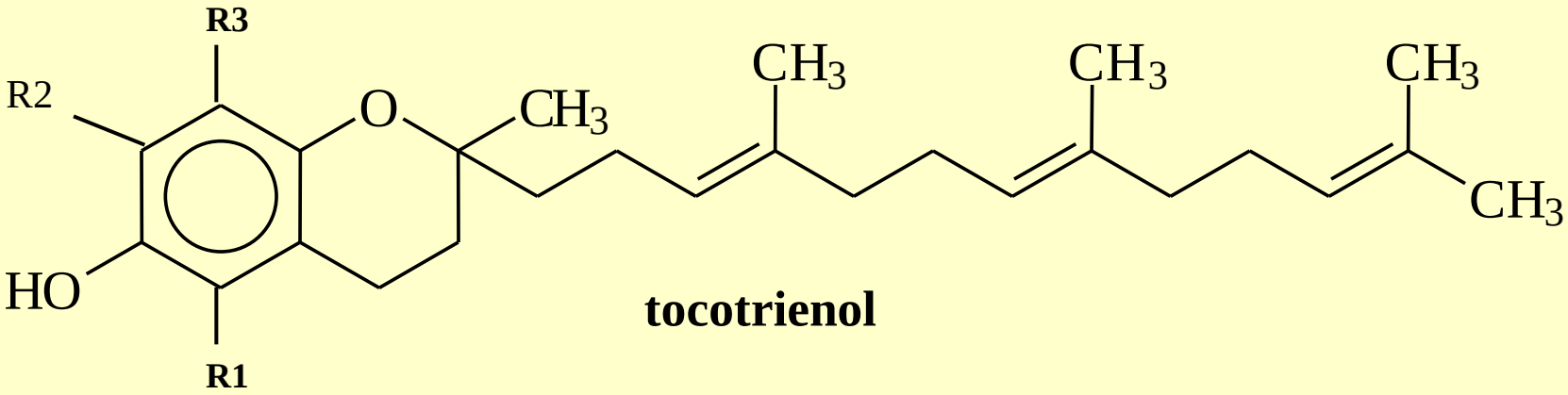


	R1	R2	R3
Tocol α	$-CH_3$	$-CH_3$	$-CH_3$
β	$-CH_3$	-H	$-CH_3$
γ	-H	$-CH_3$	$-CH_3$
δ	-H	-H	$-CH_3$

Chromanol ring

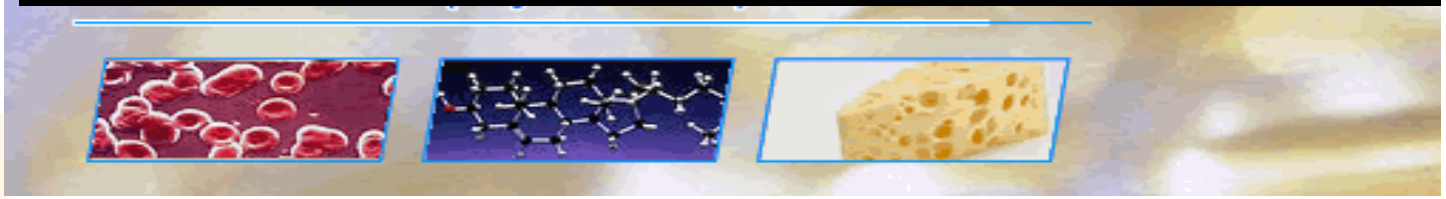
HO- group - reduction of free radicals

Saturated side chain – penetration in membranes



tocotrienol

VITAMIN K - QUINONES

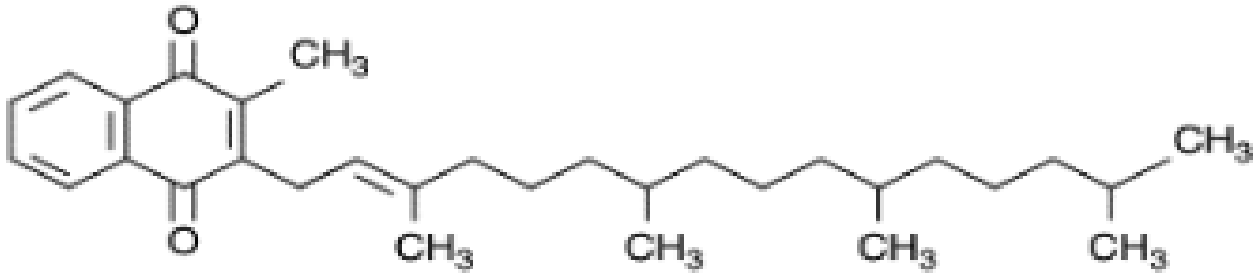


Vitamin K1 (phylloquinone) - from plant sources

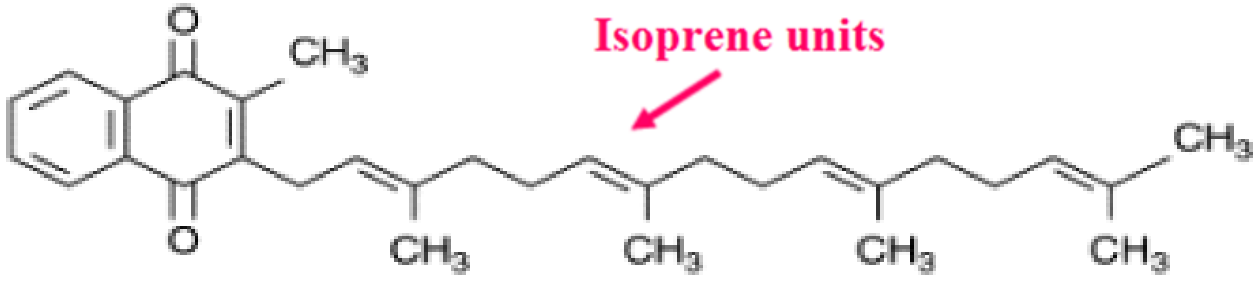
Vitamin K2 (menaquinone) - made by intestinal bacteria (production can be disturbed by antibiotics, Crohn disease)

Vitamin K3 (menadione, menadiol) - synthetic form

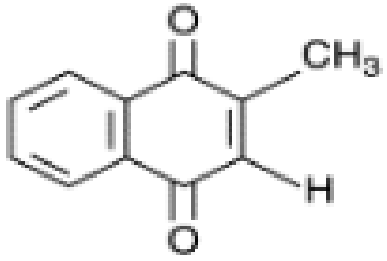
German „koagulation“ → vitamin K



Phylloquinone (vitamin K_1)



Menaquinone-4 (vitamin K_2)



Menadione (vitamin K_3)

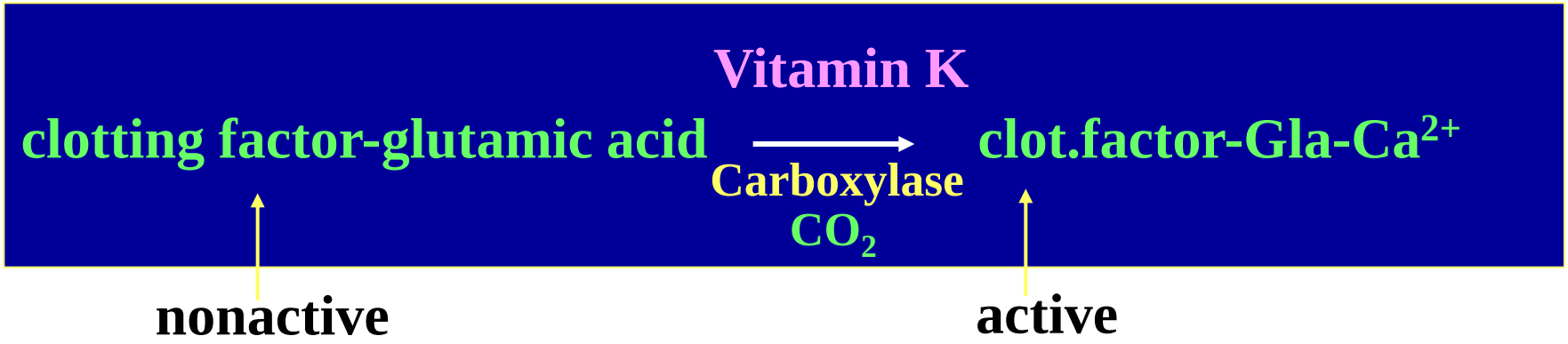
Methylated naftoquinone ring

Overview

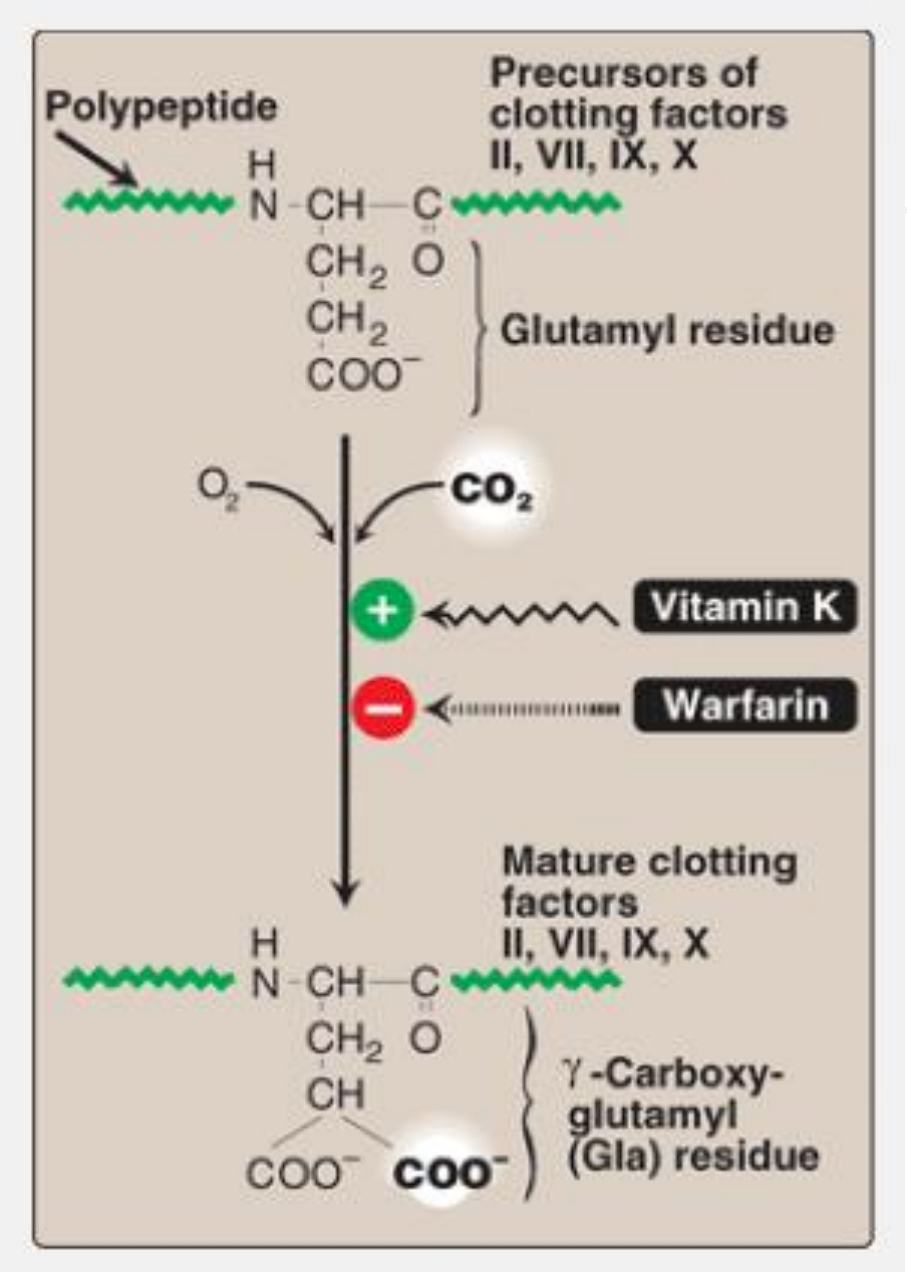
- Promotes normal blood clotting (coagulation)
- Bone metabolism
- Vascular health

Biochemistry

coenzyme of an enzyme **carboxylase** –
carboxylation of glutamic acid → gamma-carboxyglutamic acid (**Gla**) – involved in binding Ca^{2+}



Glutamate carboxylation



Deficiency

Adults at risk:

- those taking vitamin K antagonist - anticoagulant drugs
- adults with significant liver damage
- newborn babies – exclusively breast-fed:

1) vitamin K is not easily transported across the placental barrier

2) the newborn's intestines are not yet colonized with bacteria that synthesize menaquinones

VITAMIN F

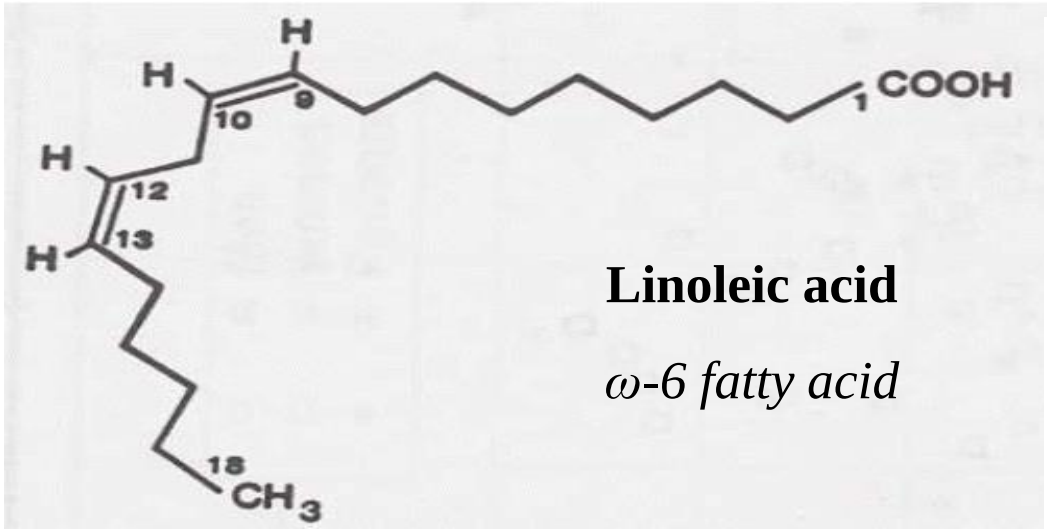
ESSENTIAL UNSATURATED HIGHER CARBOXYLIC ACIDS

Structure: unsaturated higher carboxylic acids

- **Linoleic acid -** 2 double bonds 18:2
- **Linolenic acid -** 3 double bonds 18:3
- **Arachidonic acid??? –** 4 double bonds 20:4– synthesized from linoleic acid in the body

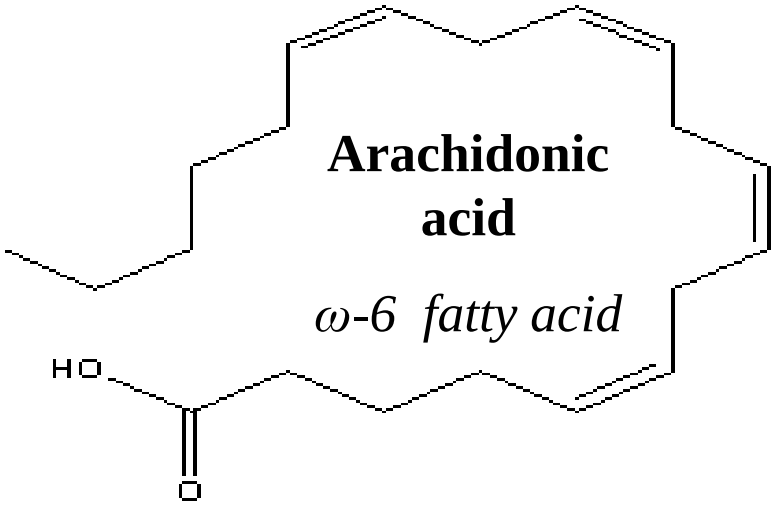
Fatty acids needed for:

normal growth, behavior, healthy cell membranes, well balanced hormone level, immune system



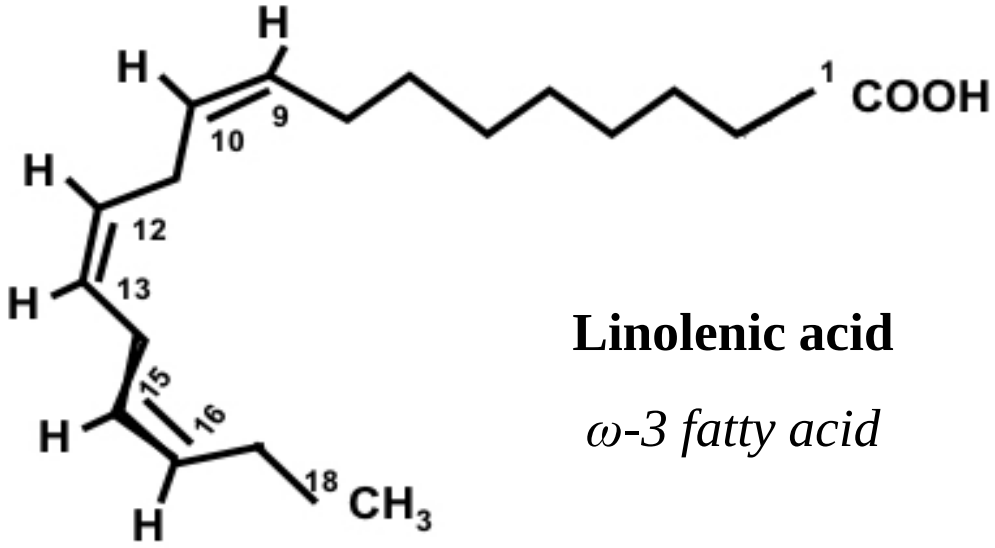
Linoleic acid

ω-6 fatty acid



Arachidonic acid

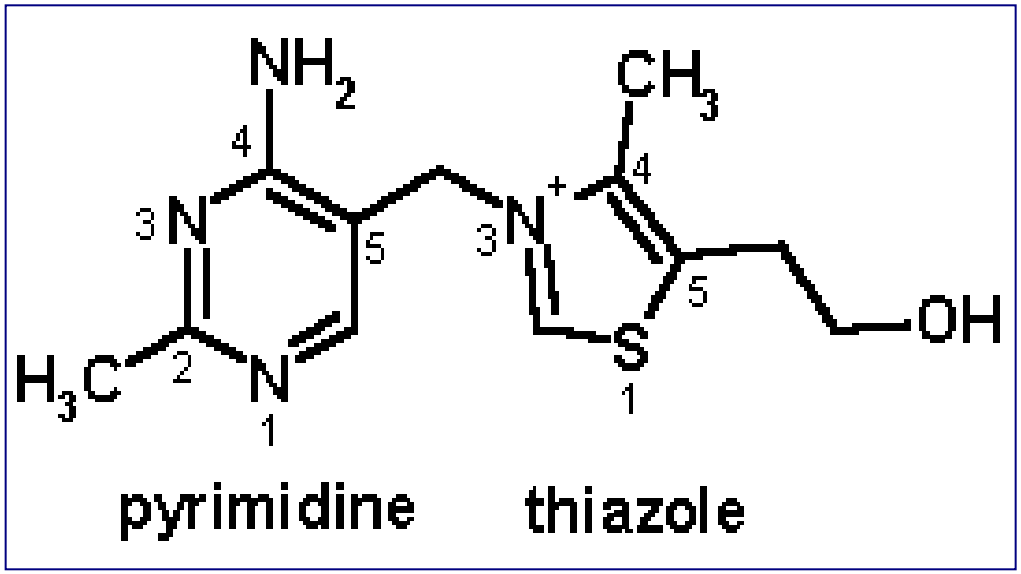
ω-6 fatty acid



Linolenic acid

ω-3 fatty acid

VITAMIN B_1 – THIAMINE, ANEURINE (antineuritic factor, antiberiberi factor)



PYRIMIDINE and THIAZOL rings linked through methylene bridge

thiamin pyrophosphate kinase

thiamin + ATP → TPP + AMP

Thiamine diphosphate

TDP - **cofactor** for several enzymes (pyruvate dehydrogenase, alpha-ketoglutarate dehydrogenase) - in catabolism of saccharides and aminoacids

Deficiency

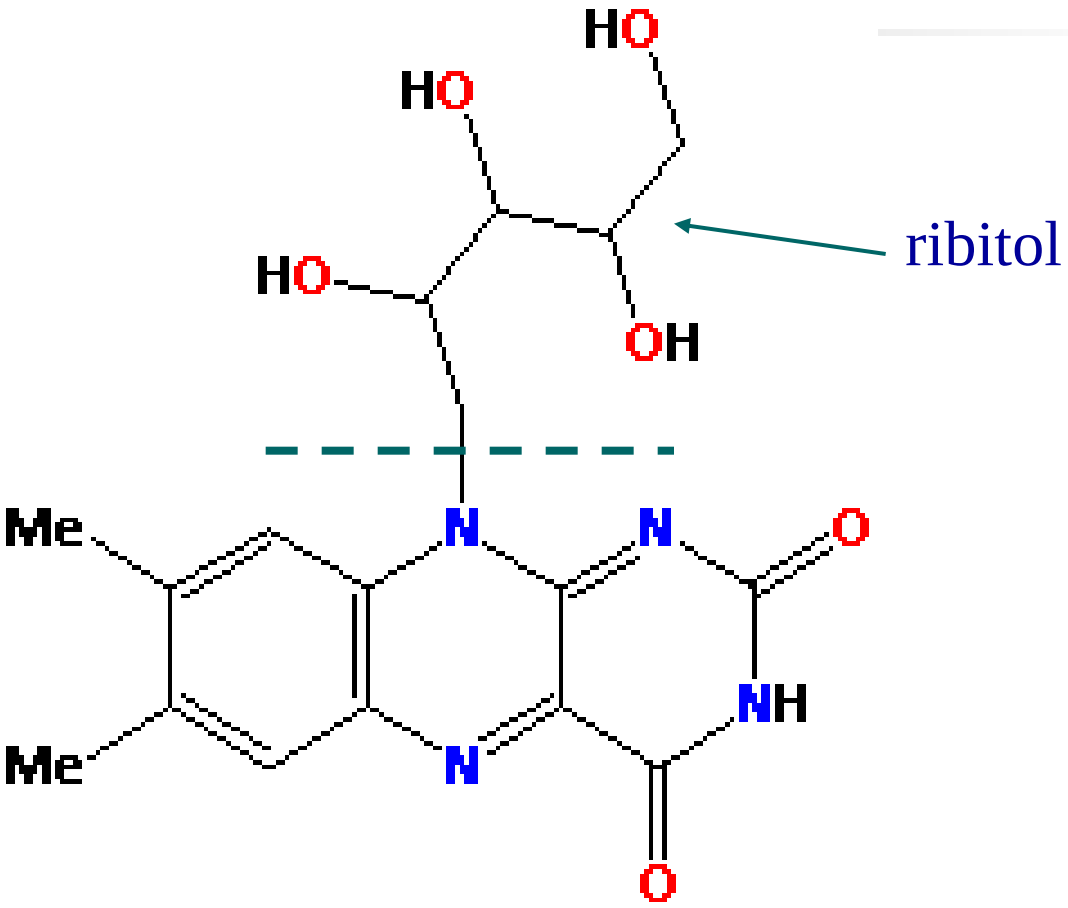
- severely reduced capacity of cells to generate energy
- **BERI-BERI** - affecting the peripheral nervous system (polyneuritis) and/or the cardiovascular system, with fatal outcome

VITAMIN B_2 – RIBOFLAVIN

Lactoflavin, ovoflavin, vitamin G

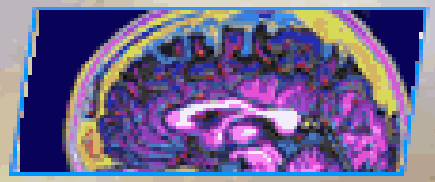
Riboflavin powder.

Riboflavin solution



METHYL DERIVATE OF ISOALOXAZINE + RIBITOL

Vitamin B2, Riboflavin

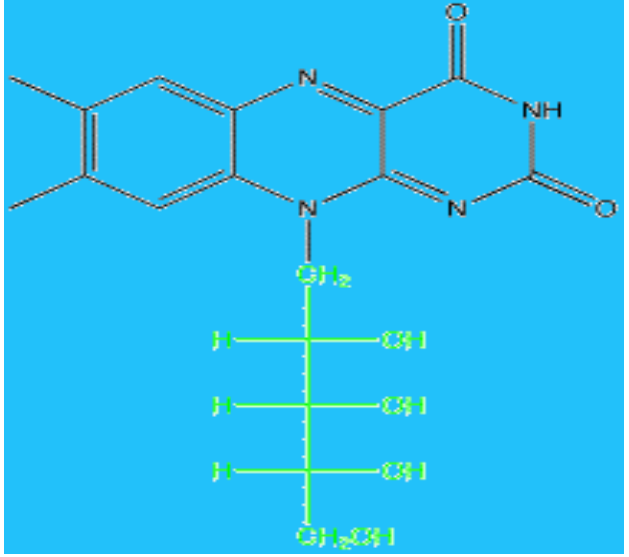


Overview

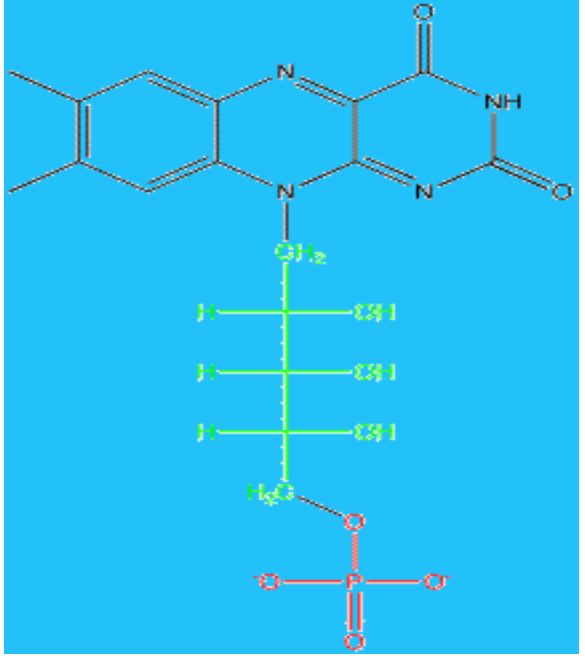
Essential to energy generation

Riboflavin - precursor for the coenzymes FAD, FMN – redox reactions

FLAVIN MONONUCLEOTIDE (FMN)
FLAVIN ADENINE DINUCLEOTIDE (FAD)

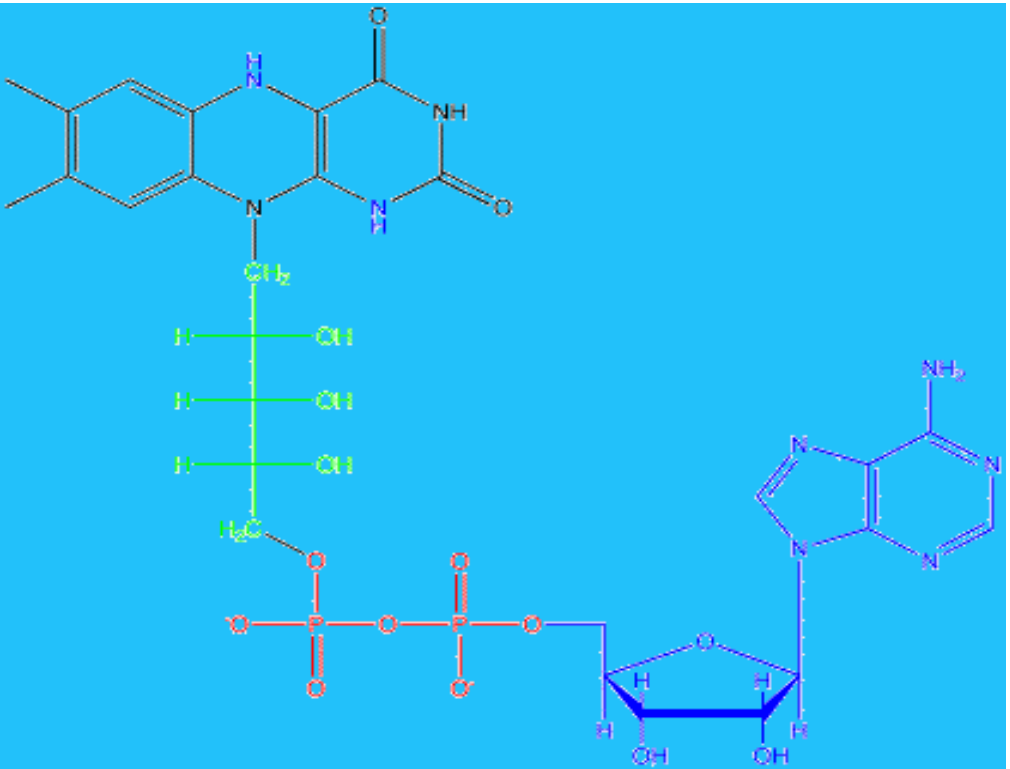


Riboflavin



Flavinmononucleotide

(FMN)

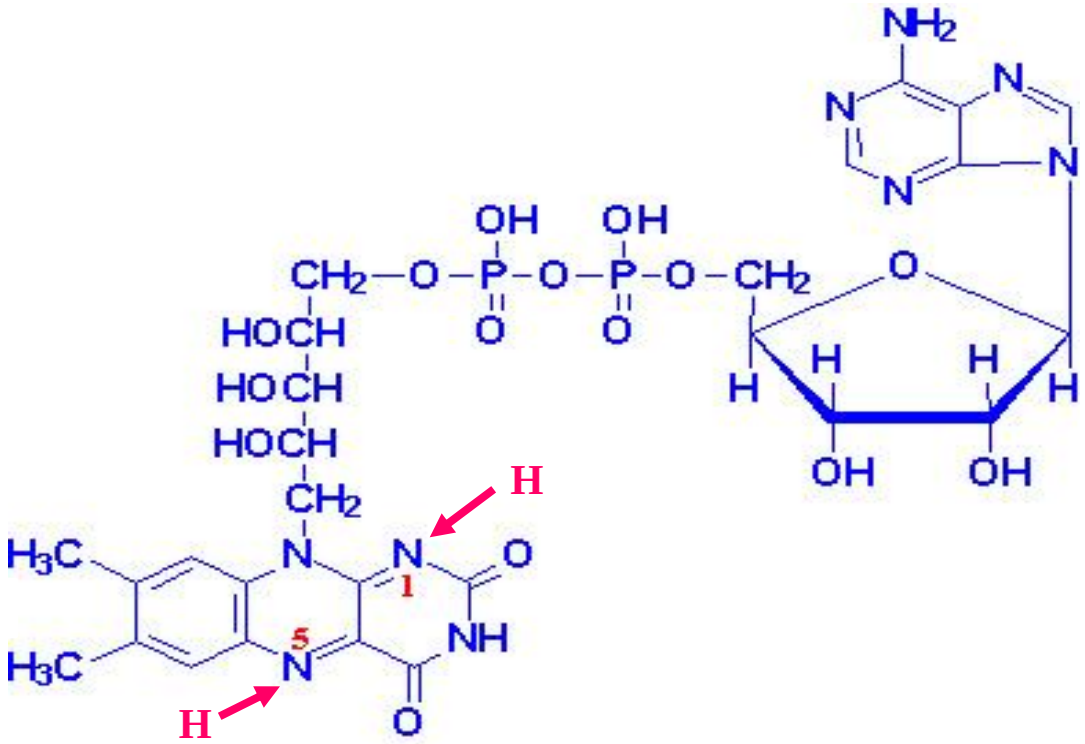


Flavinadenine dinucleotide reduc.

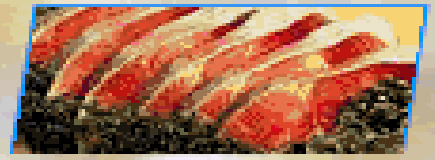
($FADH_2$)

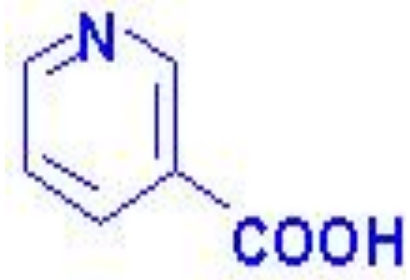
FAD

Nitrogens 1 & 5 transfer hydrogen in $FADH_2$

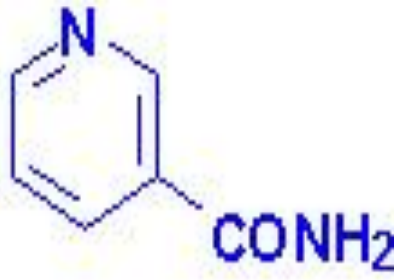


Vitamin B3, Niacin, vitamin PP





Nicotinic Acid

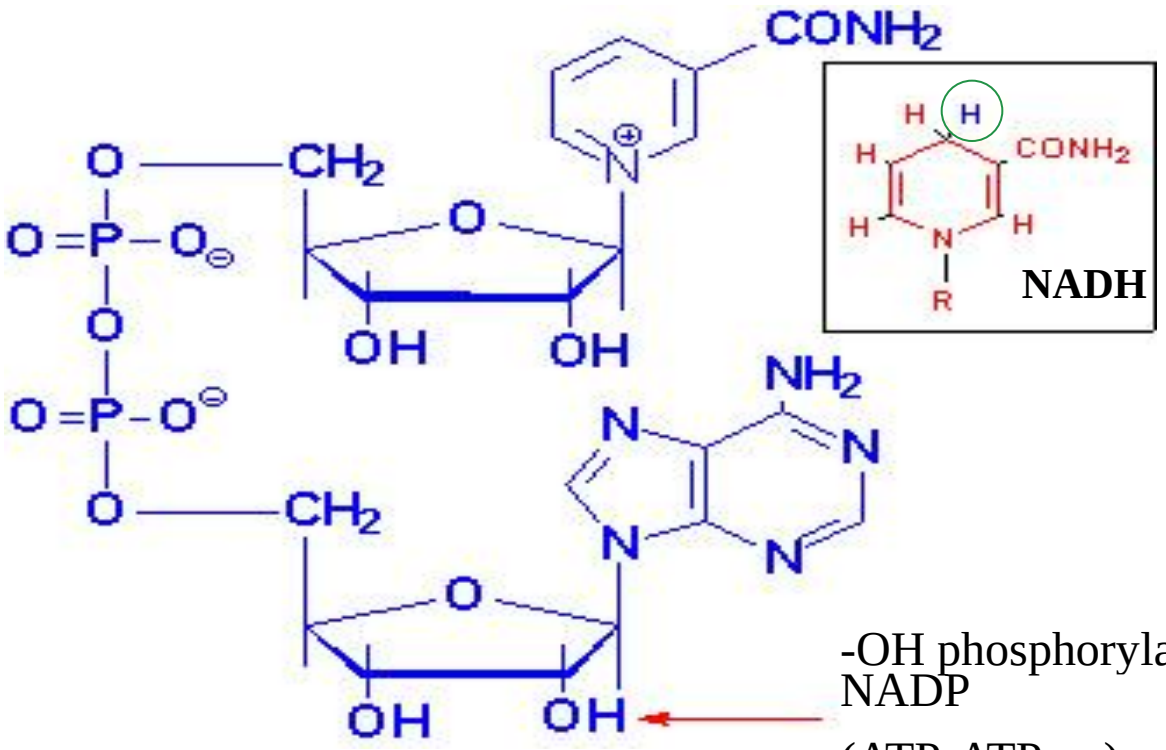


Nicotinamide

nicotinic **ac**id + vitam**in**

Niacin is not a true vitamin in the strictest definition since it can be derived from **tryptophan**.

Nicotinamide adenine dinucleotide (NAD^+) **and** **Nicotinamide adenine dinucleotide phosphate ($NADP^+$)** - cofactors for numerous dehydrogenases (lactate, malate dehydrogenases) - acceptor of H^- during alcohol oxidation



NICOTINAMIDE ADENINE DINUCLEOTIDE (NAD+)

Deficiency

Dermatitis on the hands and face, weakness

The severe symptoms, depression, dermatitis and diarrhea - **PELLAGRA (**3D disease)

PELLAGRA

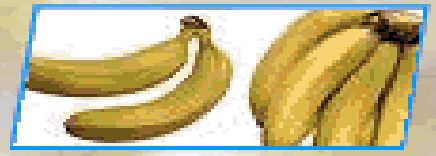
Vitamin B3
An inability to absorb niacin (vitamin B3) or the amino acid tryptophan may cause pellagra, a disease characterized by scaly sores, mucosal changes and mental symptoms.
A.D.A.M.

GLOVE-AND-STOCKING

Overdose

Niacin flush, liver damage, stomach ulcers, nausea, diarrhea, weakness

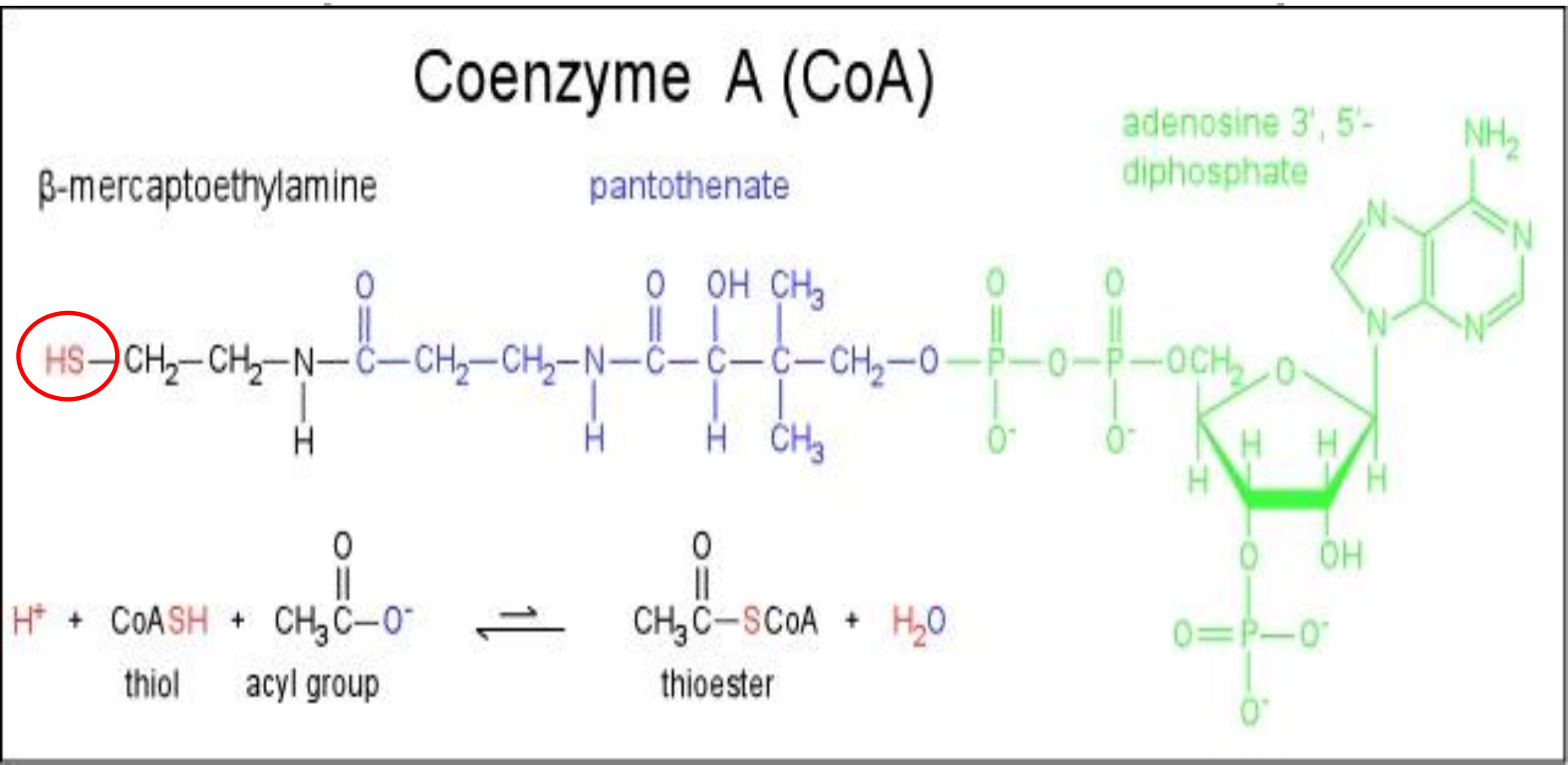
Vitamin B5 – Pantothenic Acid



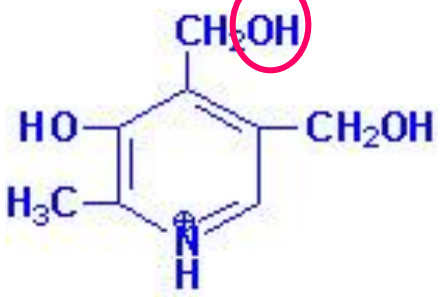
Overview

- Pantothenate is required for synthesis of **coenzyme A** – metabolism of saccharides, proteins, lipids.

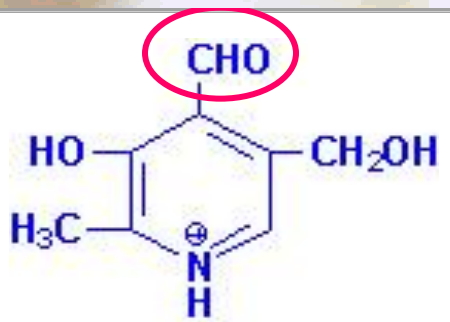
Coenzyme A (CoA)



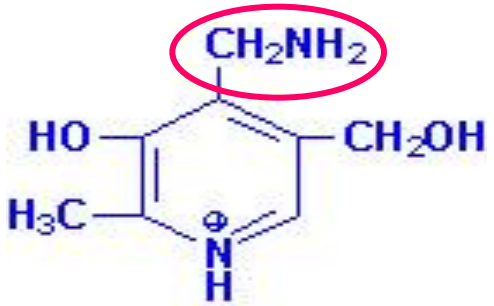
Vitamin B6 – Pyridoxine



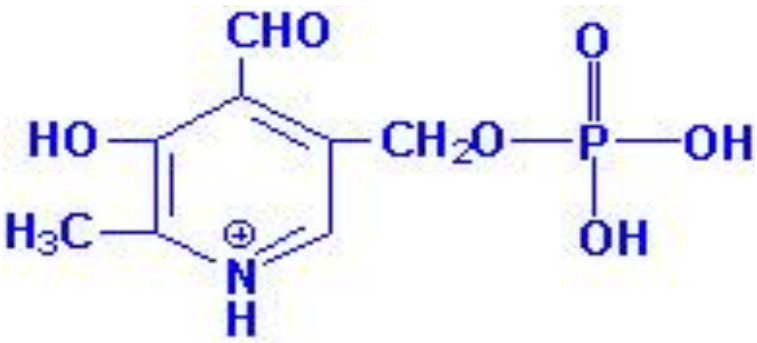
Pyridoxine (Pyridoxol)



Pyridoxal



Pyridoxamine



Pyridoxal Phosphate (PDP)

All three compounds are efficiently converted to the biologically active form of vitamin B_6, **PYRIDOXAL PHOSPHATE (PDP)**

Functions of vitamin B6

- **Affects the body's use of proteins, saccharides**
  - a coenzyme in all transamination reactions, in some decarboxylation and deamination of amino acids

- **PDP aids in the synthesis of heme**

- **Helps in absorption of vitamin B_{12} and formation of erythrocytes**

- **Role in the conversion of tryptophan to serotonin – help against mental depression**

$$\text{tryptophan} \xrightarrow{\text{B6}} \text{serotonin}$$

Deficiency

- Anemia
- Nerve damage (mental confusion, irritability, nervousness)
- Skin problems
- Sores in the mouth

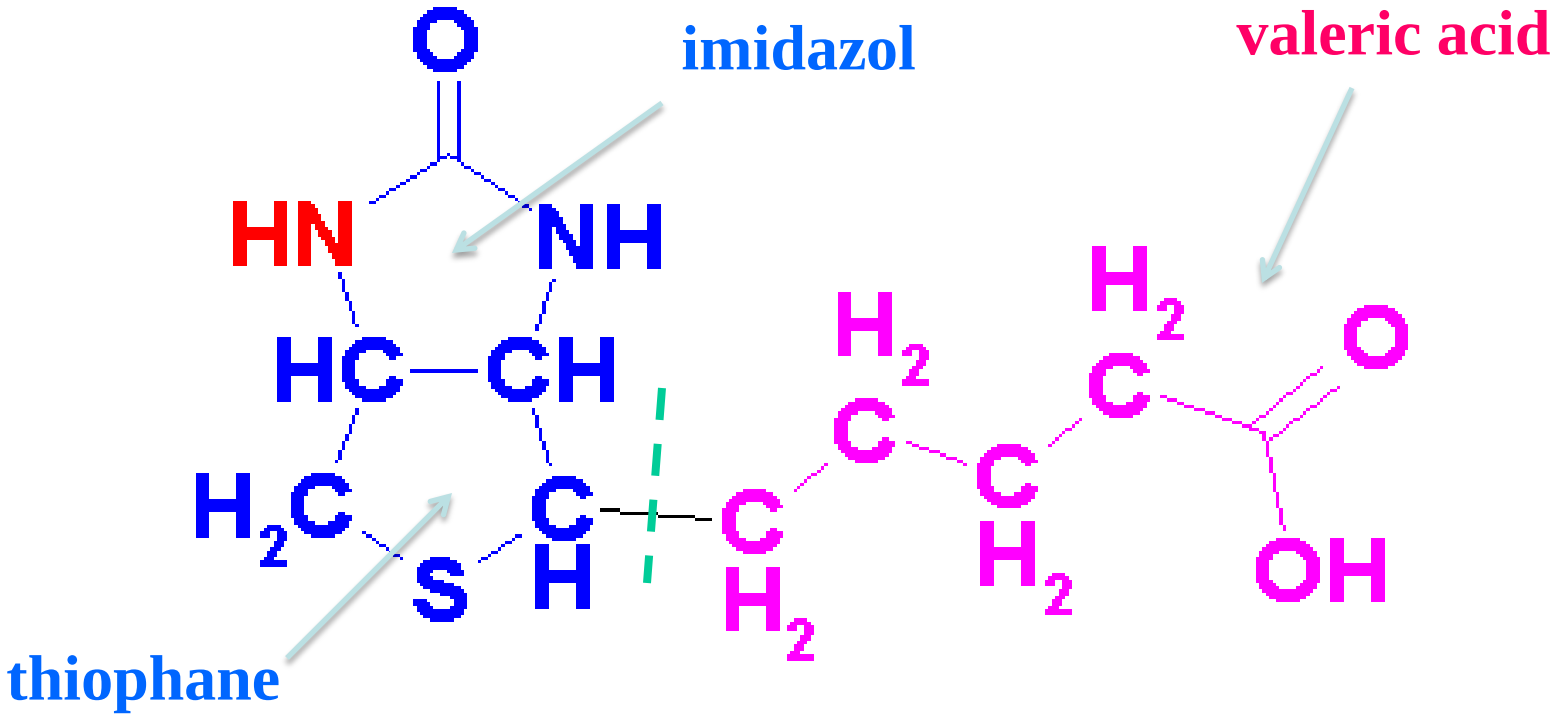
Deficiencies of vitamin B_6 are rare

VITAMIN H - BIOTIN

FUNCTION

- **Cofactor** of enzymes that are involved in **CARBOXYLATION** reactions (e.g. acetylCoA carboxylase, pyruvate carboxylase)

  - helps to transfer CO_2



STRUCTURE - imidazol and thiophane heterocyclic ring with valeric acid

DEFICIENCY

- hair loss,
- depression, halucination,
- muscle pain,
- dermatitis

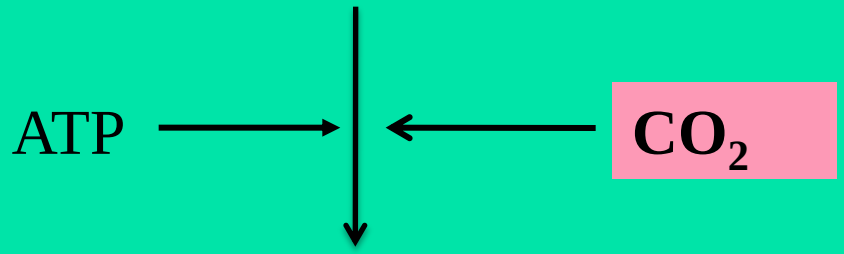
Synthetized by intestinal bacteria - deficiencies rare

Raw eggs - **avidin from egg whites + biotin = complex**

preventing absorption of biotin → vit. H deficiency

COENZYME - BIOCYTIN

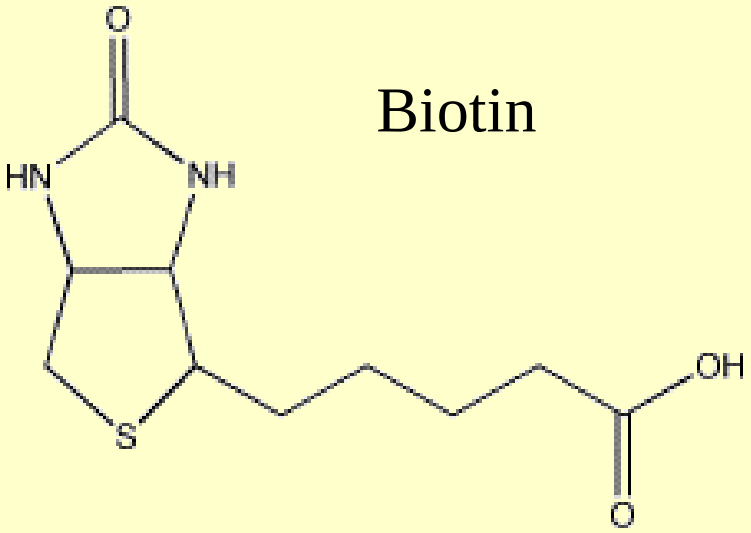
Biotin + Lysin-enzyme = Biocytin (biotinyllysin)



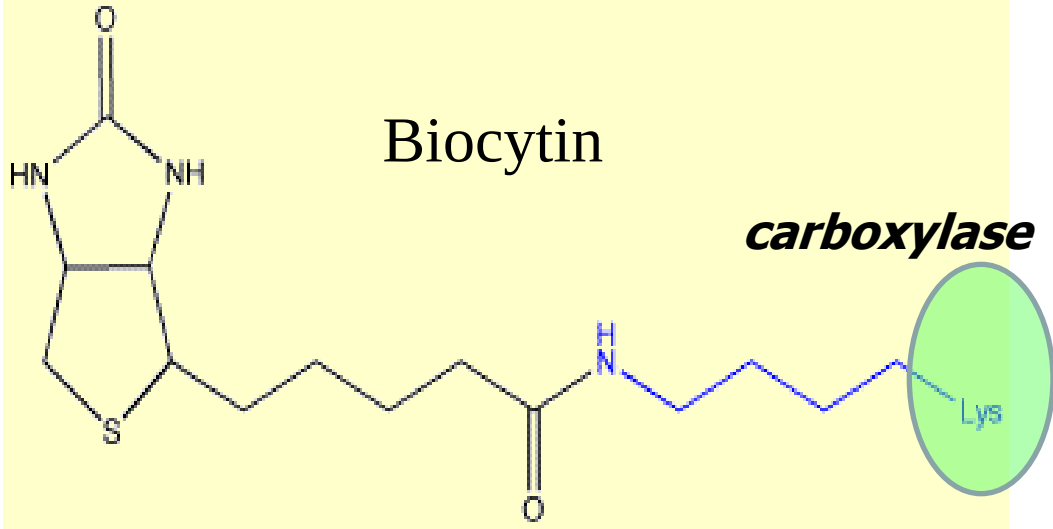
carboxybiocytin

- Coenzyme of **carboxylases** – enzymes transporting CO_2

Biotin

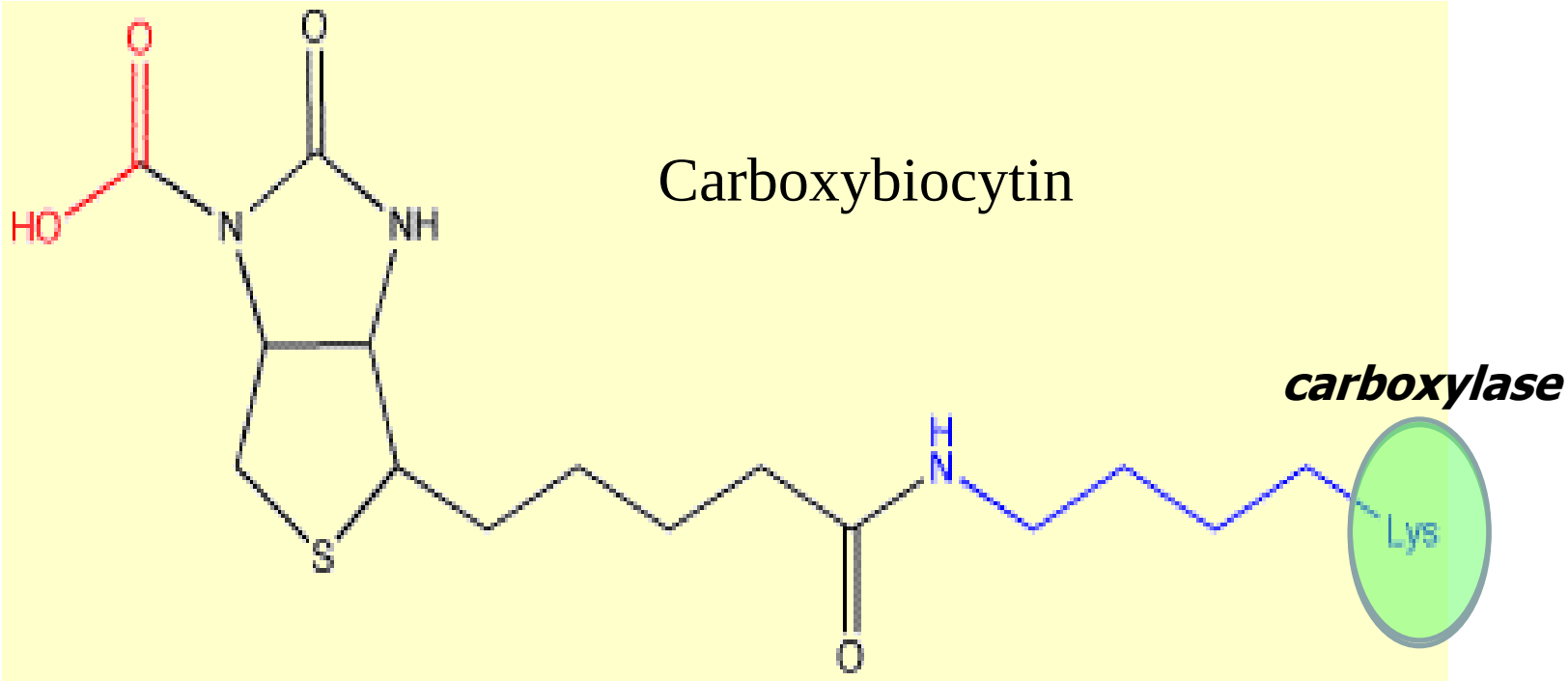


Biocytin



carboxylase

Carboxybiocytin



carboxylase

Vitamin B_9 - Folic Acid

Folacin

Overview

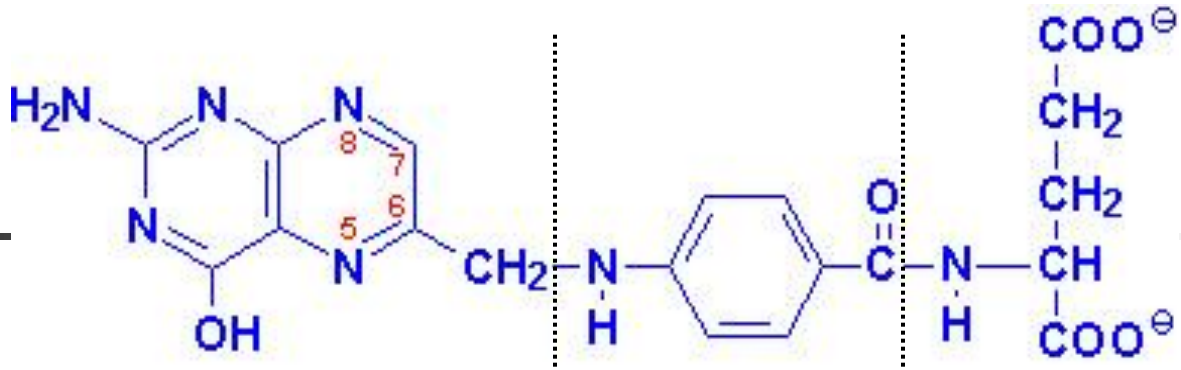
- Nucleotide biosynthesis
- DNA and RNA synthesis and repair
- Cofactor in biological reactions involving folate
- Important during periods of rapid cell division and growth
- Production of red blood cells, prevention of anemia.

Benefits

To **transfer** various forms of **one carbon units** (methyl, methylene, methenyl, formyl or formimino groups) during biosynthetic reactions (purine nucleotides, dTMP)

Promotes a healthy pregnancy

pterin PABA Glutamic acid



Folic Acid

positions 7 & 8 carry hydrogens in dihydrofolate (DHF)
positions 5-8 carry hydrogens in tetrahydrofolate (THF)

- Active form of folic acid - **tetrahydrofolate (THF) – coenzyme F** – formylating coenzyme – transfer of 1-carbon moeities

- **PABA** (para-aminobenzoic acid)- vitamin character – not synthetized in the organism

Deficiency

Neural tube defects in developing embryos

Megaloblastic anaemia

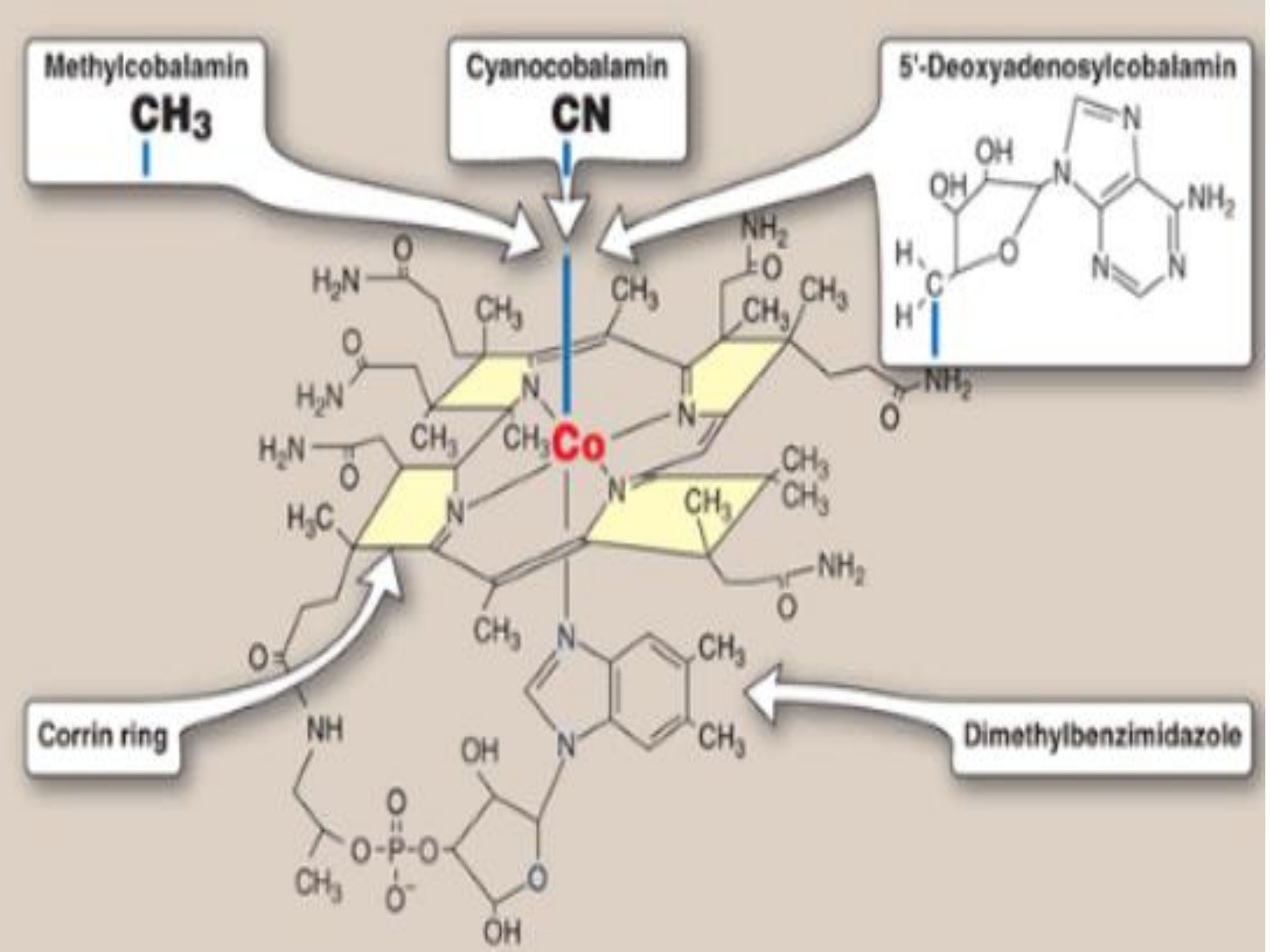
Spina bifida

- Malformation of the spine
- Lost ability to control bladder - urination,
- Impaired function of legs

VITAMIN B_{12} - Cyanocobalamin

Function

- Synthesis of DNA and erythrocytes
- Proper function of brain and nervous system

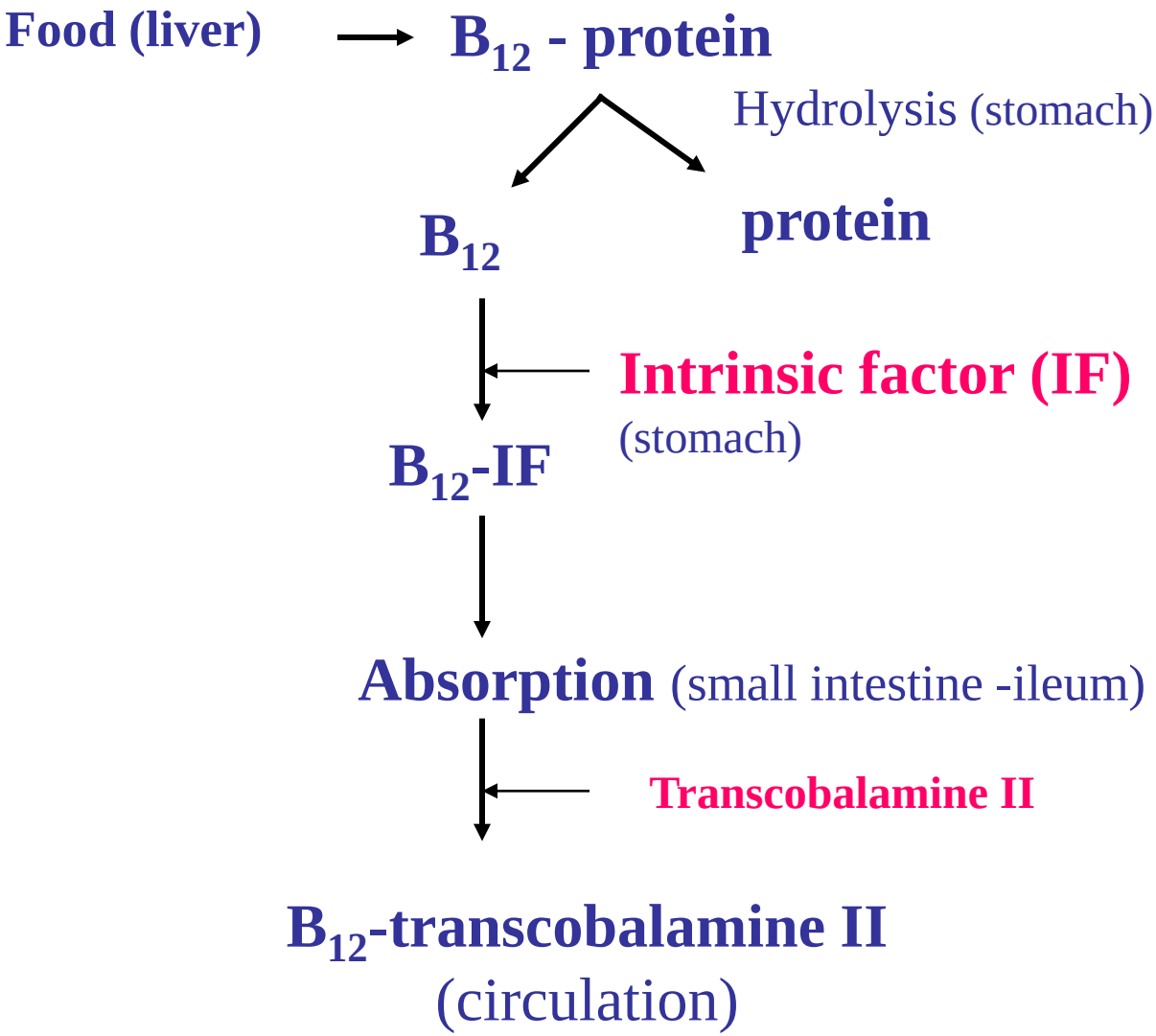

Methylcobalamin
CH3
Cyanocobalamin
CN
5'-Deoxyadenosylcobalamin
Co
Corrin ring
Dimethylbenzimidazole

Deficiency

- **Pernicious anaemia**
- Nausea, loss of appetite, sore mouth

Deficiencies - rare

The liver can store vitamin B12 for up to six years


Food (liver)
B12 - protein
Hydrolysis (stomach)
B12
protein
Intrinsic factor (IF)
(stomach)
B12-IF
Absorption (small intestine -ileum)
Transcobalamine II
B12-transcobalamine II
(circulation)

Binding of **B12-transcobalamin** II to the cell receptors

↓

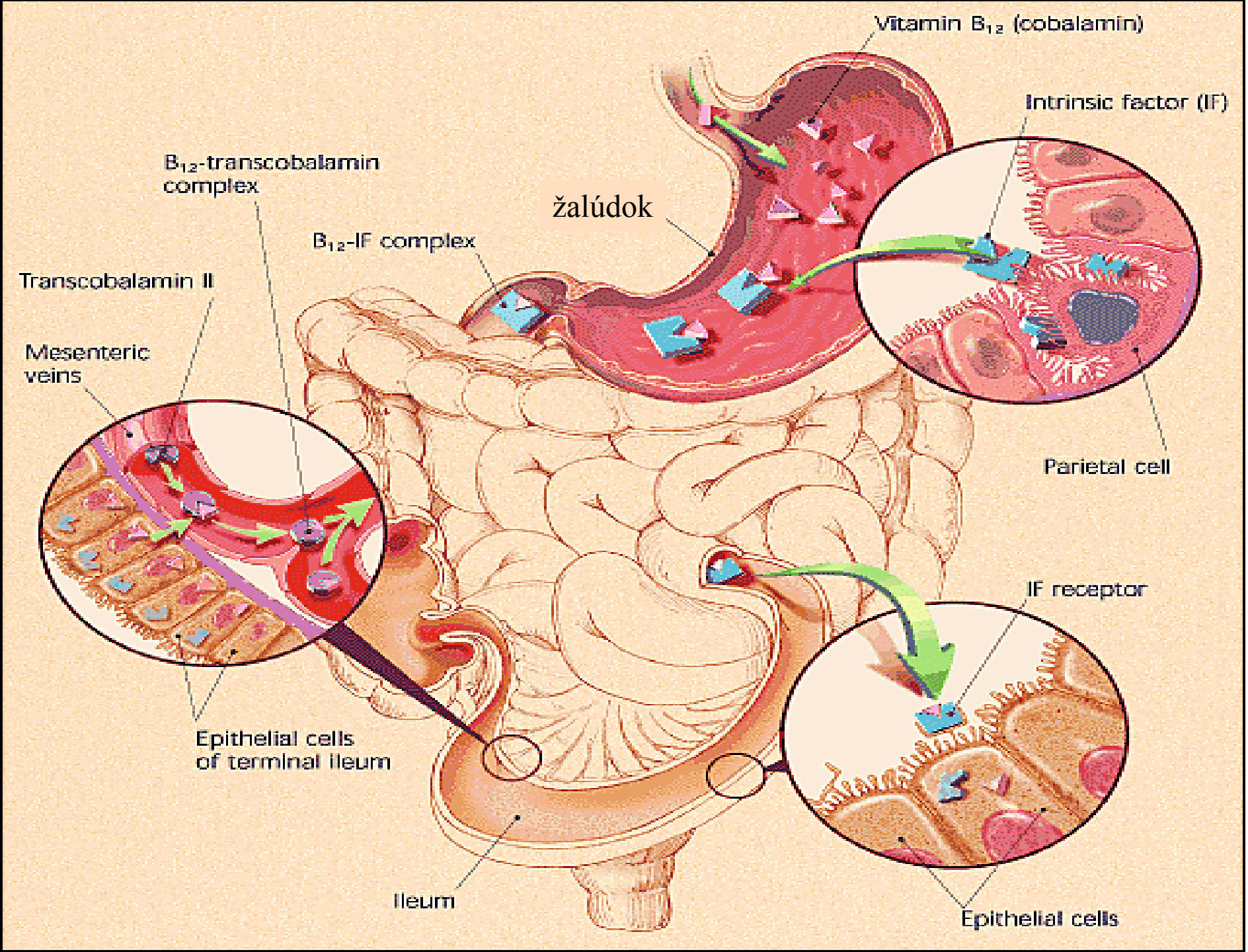
Endocytosis of the complex into cells

↓

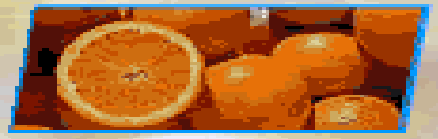
Degradation of the complex in lysosomes and liberation of B12

↓

Coenzyme of enzymes in the cell cytoplasm

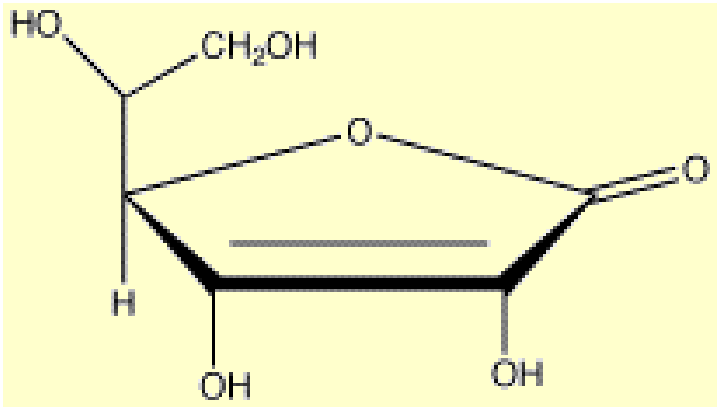

Vitamin B_{12} (cobalamin)
Intrinsic factor (IF)
B_{12}-transcobalamin complex
žalúdok
B_{12}-IF complex
Transcobalamin II
Mesenteric veins
Parietal cell
IF receptor
Epithelial cells of terminal ileum
Ileum
Epithelial cells
© 2003 JOAN M. BECK

Vitamin C (Ascorbic Acid)

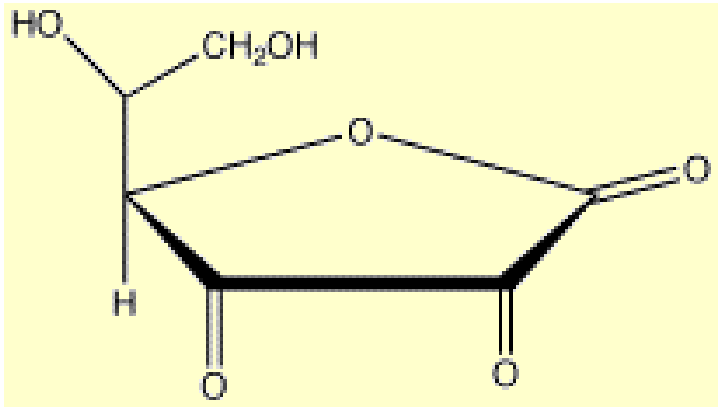


Overview

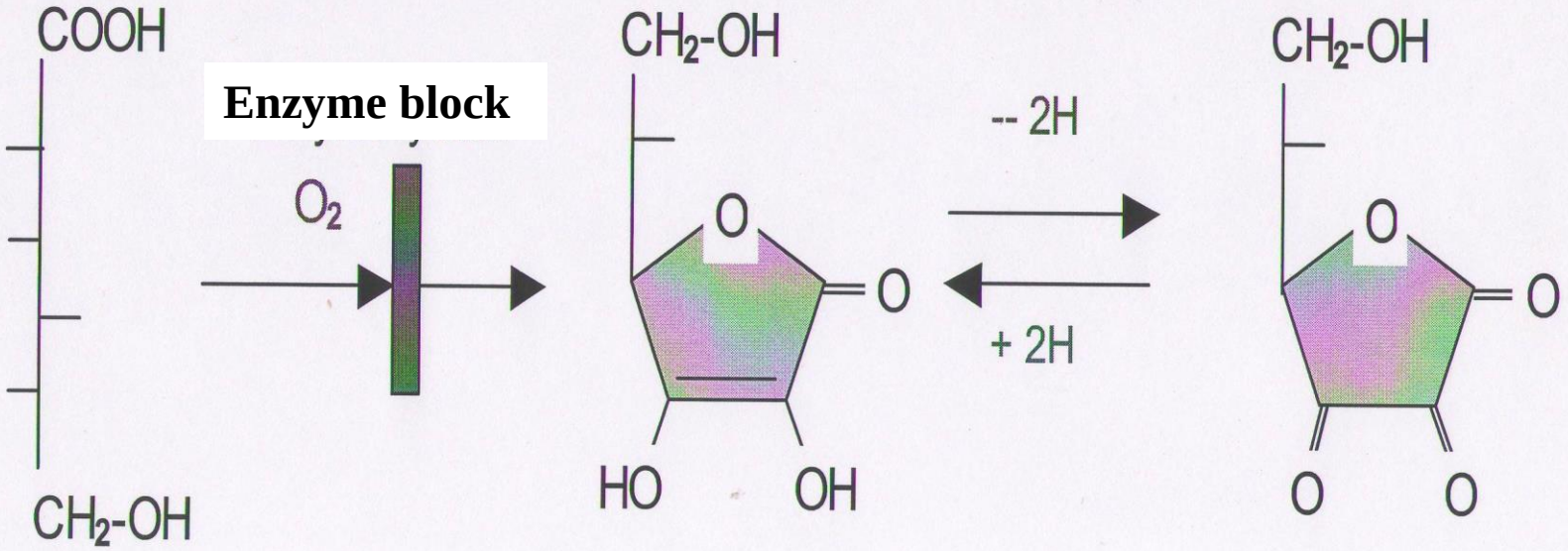
Participates in oxidation-reduction reactions



Ascorbic acid



Dehydroascorbic acid



Gulonic acid

L-ascorbic acid

L-dehydroascorbic acid

- The vast majority of animals and plants are able to synthesize their own ascorbic acid (excluding humans, guinea pigs, bats)

FUNCTION

- ✓ Antioxidant (prooxidant)
- ✓ Cofactor of enzymes used in the synthesis of collagen
- ✓ Tyrosine degradation
- ✓ Adrenalin synthesis
- ✓ Carnitin synthesis
- ✓ Bile acids production
- ✓ Steroidogenesis
- ✓ Iron absorption

Deficiency

Muscle weakness, swollen gums, loss of teeth, tiredness

Scurvy - avitaminosis

Liver spots on the skin

Spongy gums

SCURVY