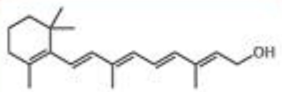
VITAMINS

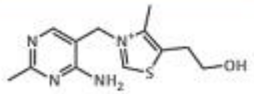
VITAMIN A



RETINOL
active form in mammalian tissues

Important for eyesight. Also strengthens immune system and keeps skin and linings of parts of the body healthy.

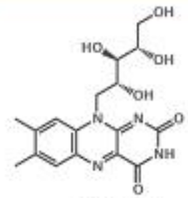
VITAMIN B1



THIAMIN
can also occur in pyrophosphate ester form

Used to keep nerves & muscle tissue healthy. Also important for processing of carbohydrates and some proteins.

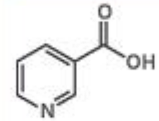
VITAMIN B2



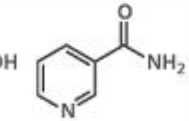
RIBOFLAVIN
excess turns urine bright yellow

Important for body growth, red blood cell production, and keeping the eyes healthy. Also helps processing of carbohydrates.

VITAMIN B3



NICOTINIC ACID

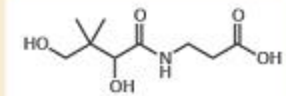


NICOTINEAMIDE

niacin is collective name for these compounds

Helps with digestion and digestive system health. Also helps with the processing of carbohydrates.

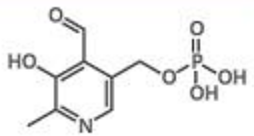
VITAMIN B5



PANTOTHENIC ACID
also occurs in pyrophosphate ester form

Important for manufacturing red blood cells and maintaining a healthy digestive system. Also helps process carbohydrates.

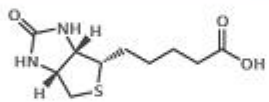
VITAMIN B6



PYRIDOXAL PHOSPHATE
active form in mammalian tissues

Helps make some brain chemicals; needed for normal brain function. Also helps make red blood cells and immune system cells.

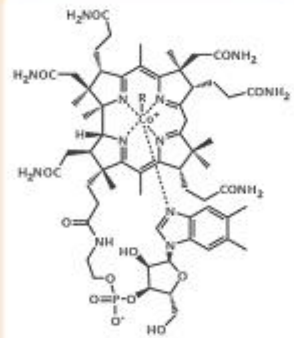
VITAMIN B7



BIOTIN
produced by intestinal bacteria

Needed for metabolism of various compounds. Often recommended for strengthening hair, but evidence is variable.

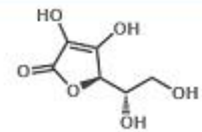
VITAMIN B12



COBALAMIN
usually contains CN as the R group

Important for the nervous system, for making red blood cells, and helps in the production of DNA and RNA.

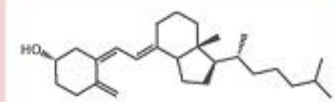
VITAMIN C



ASCORBIC ACID
deficiency can cause scurvy

Important for a healthy immune system; helps produce collagen, used to make skin and other tissues. Also helps wound healing.

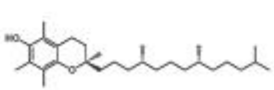
VITAMIN D



CHOLECALCIFEROL
natural form; different form used in supplements

Important for bone health and maintaining the immune system function. May also have a preventative role in cancers.

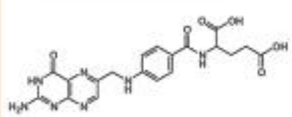
VITAMIN E



ALPHA-TOCOPHEROL
group includes tocopherols & tocotrienols

An antioxidant that helps prevent damage to cells and may have a preventative role in cancer. Also helps make red blood cells.

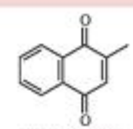
VITAMIN B9



FOLIC ACID
found as tetrahydrofolate in food

Important for brain function & mental health. Aids production of DNA & RNA. Important when tissues are growing quickly.

VITAMIN K



MENADIONE
all K vitamins are menadione or derivatives

Helps blood clot properly, & plays a key role in bone health. Newborns receive vitamin K injections to prevent bleeding.

Key

Vitamins can be divided broadly into two classes.

WATER-SOLUBLE VITAMINS
These vitamins are not stored in the body. As such, generally, they are required more frequently than the fat-soluble vitamins.

FAT-SOLUBLE VITAMINS
These vitamins are stored in the liver and fatty tissues until required. As such, they can be harmful if too much is taken in.

❖Vitamins are defined as a group of complex organic compounds present in minute amounts in natural foodstuffs that are essential to normal metabolism and lack of which in the diet causes deficiency diseases.

❖Vitamins consist of a mixed group of chemical compounds and are not related to each other as are proteins, carbohydrates, and fats.

❖Their classification together depends not on chemical characteristics but on function.

❖Vitamins are required in trace amounts (micrograms to milligrams per day) in the diet for health, growth, and reproduction.

❖Omission of a single vitamin from the diet of a species that requires it will produce deficiency signs and symptoms.

❖Many of the vitamins function as coenzymes (metabolic catalysts); others have no such role, but perform certain essential functions.

❖Classically, vitamins have been divided into two groups based on their solubilities in fat solvents or in water.

❖Thus, fat-soluble vitamins include A, D, E, and K, while vitamins of the B-complex and C are classified water soluble.

❖Fat-soluble vitamins are found in foodstuffs in association with lipids. The fat-soluble vitamins are absorbed along with dietary fats, apparently by mechanisms similar to those involved in fat absorption.

❖Conditions favorable to fat absorption, such as adequate bile flow and good micelle formation, also favor absorption of the fatsoluble vitamins.

❖Water-soluble vitamins are not associated with fats, and alterations in fat absorption do not affect their absorption.

❖Three of the four fat-soluble vitamins (vitamins A, D, and E) are well stored in appreciable amounts in the animal body.

❖Except for vitamin B12, water-soluble vitamins are not well stored, and excesses are rapidly excreted.

❖A continual dietary supply of the water-soluble vitamins and vitamin K is needed to avoid deficiencies.

❖Fat-soluble vitamins are excreted primarily in the feces via the bile, whereas water-soluble vitamins are excreted mainly in the urine.

❖Water-soluble vitamins are relatively nontoxic, but excesses of fat-soluble vitamins A and D can cause serious problems.

❖Fat-soluble vitamins consist only of carbon, hydrogen, and oxygen, whereas some of the water-soluble vitamins also contain nitrogen, sulfur, or cobalt.

■ **Table 1.1 Fat- and Water-Soluble Vitamins with Synonym Names**

Vitamin	Synonym
Fat soluble	
Vitamin A_1	Retinol, retinal, retinoic acid
Vitamin A_2	Dehydroretinol
Vitamin D_2	Ergocalciferol
Vitamin D_3	Cholecalciferol
Vitamin E	Tocopherol, tocotrienols
Vitamin K_1	Phylloquinone
Vitamin K_2	Menaquinone
Vitamin K_3	Menadione[a]
Water soluble	
Thiamin	Vitamin B_1
Riboflavin	Vitamin B_2
Niacin	Vitamin pp, vitamin B_3
Vitamin B_6	Pyridoxol, pyridoxal, pyridoxamine
Pantothenic acid	Vitamin B_5
Biotin	Vitamin H
Folacin	Folic acid, folate, vitamin M, vitamin B_c
Vitamin B_{12}	Cobalamin
Choline	Gossypine
Vitamin C	Ascorbic acid

[a]The synthetic form is water soluble.

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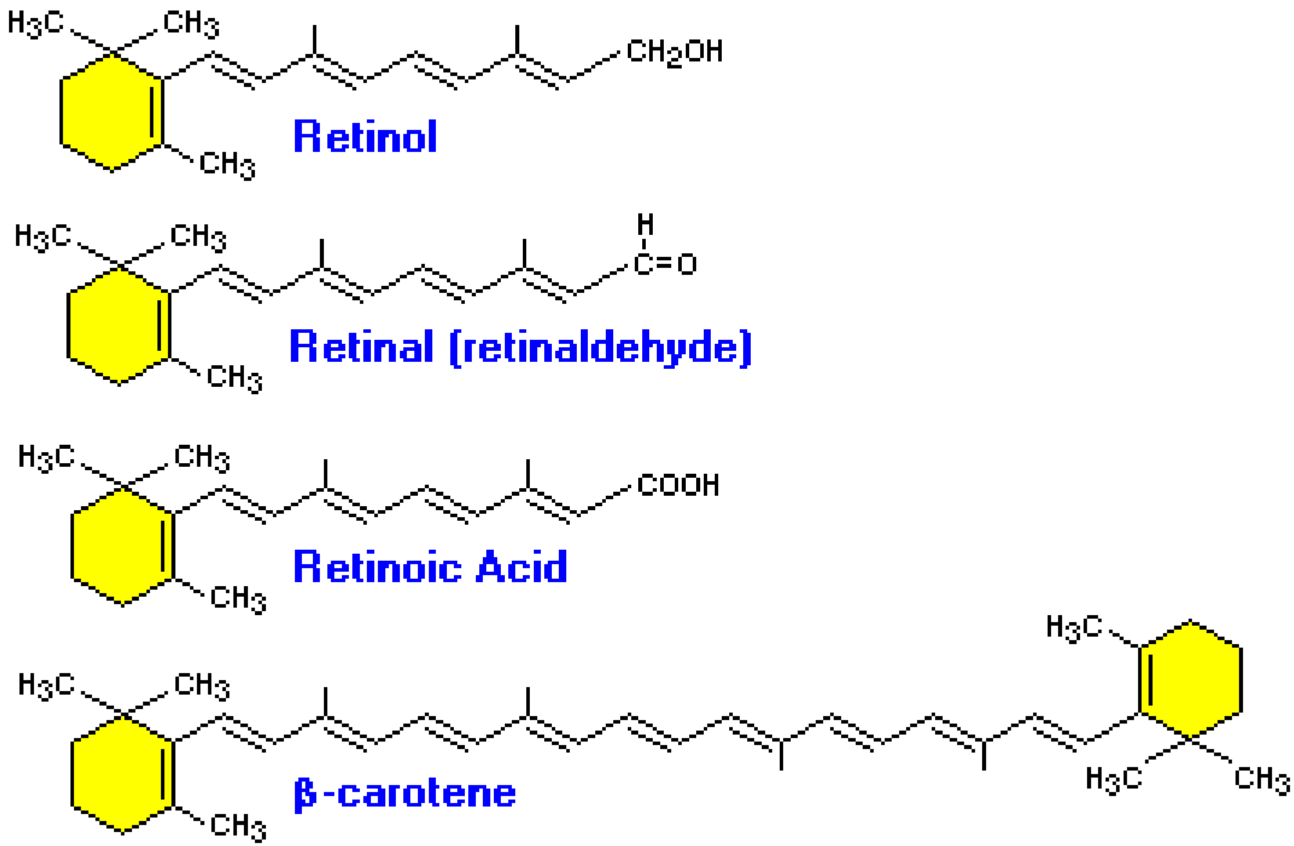
VITAMIN A

❖Although all vitamins are equally important in supporting animal life, vitamin A may be considered the most important vitamin from a practical standpoint.



❖Vitamin A itself does not occur in plants; however, its precursors (carotenoids) are found in plants, and these can be converted to true vitamin A by a specific enzyme located in the intestinal walls of animals.

❖In human nutrition, vitamin A is one of the few vitamins of which both deficiency and excess constitute a serious health hazard. Ü

❖Deficiency occurs in endemic proportions in many developing countries and is considered to be the most common cause of blindness in young children throughout the world.

❖Vitamin A toxicity usually arises from abuse of vitamin supplementation.

❖The most active vitamin A form and that most usually found in mammalian tissues is the all-trans-vitamin A.

❖Liver normally contains about 90% of total-body vitamin A.

- Vitamin A is necessary for support of growth, health, and life of higher animals.

- In the absence of vitamin A, animals will cease to grow and eventually die.

- It is of primary importance in development of young, growing animals.

- Vitamin A deficiency causes at least four different and probably physiologically distinct lesions:

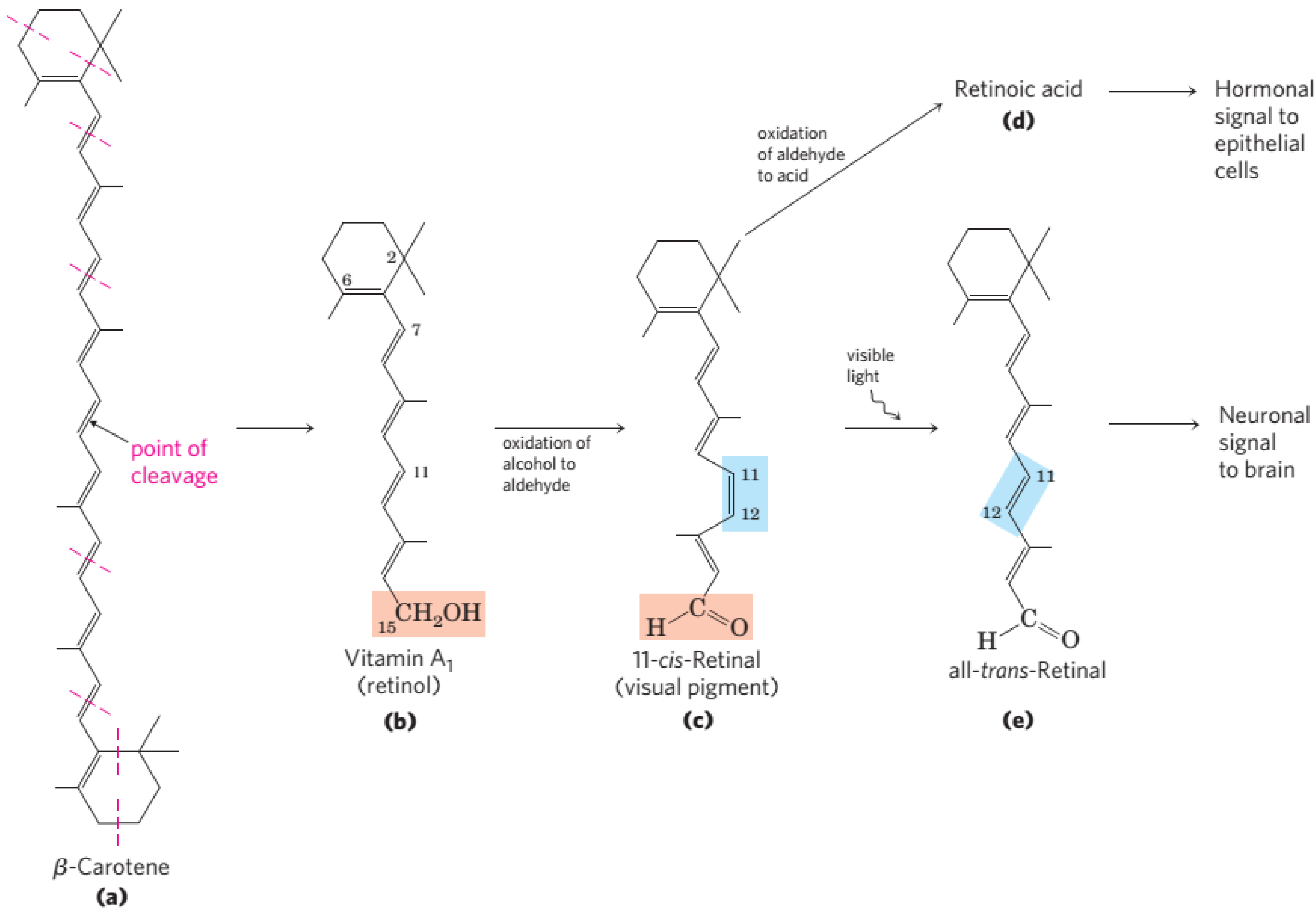
- loss of vision due to a failure of rhodopsin formation in the retina;

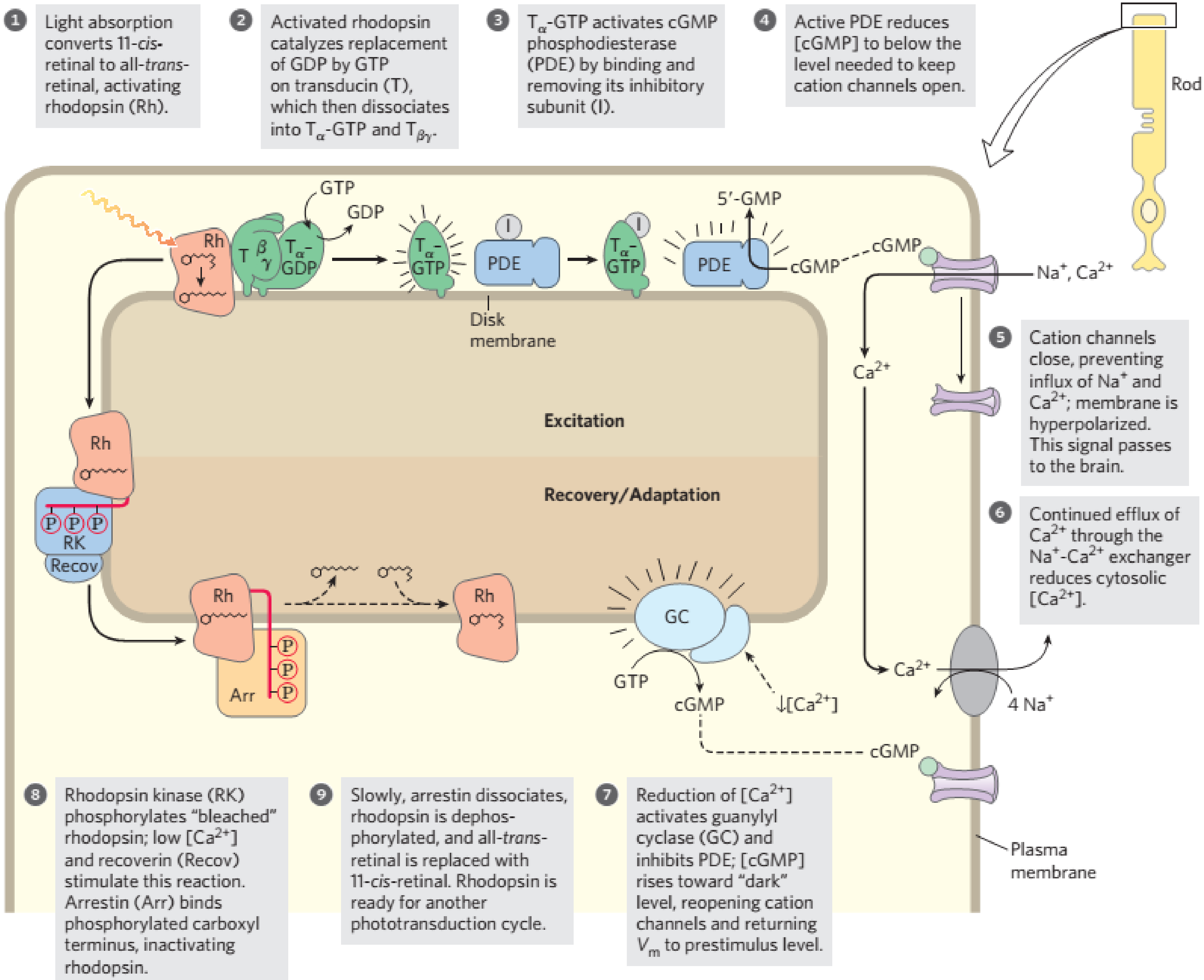
- defects in bone growth;

- defects in reproduction and

- defects in growth and differentiation of epithelial tissues, frequently resulting in keratinization.

❖Vitamin A is an essential component of vision. Vitamin A deficiency, in terms of the need for the resynthesis of rhodopsin, results in night blindness (nyctalopia).





1 Light absorption converts 11-*cis*-retinal to all-*trans*-retinal, activating rhodopsin (Rh).
2 Activated rhodopsin catalyzes replacement of GDP by GTP on transducin (T), which then dissociates into T_α-GTP and $T_{\beta\gamma}$.
3 T_α-GTP activates cGMP phosphodiesterase (PDE) by binding and removing its inhibitory subunit (I).
4 Active PDE reduces [cGMP] to below the level needed to keep cation channels open.
Rod
GTP
GDP
Rh
T
β
γ
T_α-GDP
T_α-GTP
I
PDE
5′-GMP
cGMP
Disk membrane
Na^+, Ca^{2+}
Ca^{2+}
5 Cation channels close, preventing influx of Na^+ and Ca^{2+}; membrane is hyperpolarized. This signal passes to the brain.
Excitation
Recovery/Adaptation
P P P
RK
Recov
Arr
GC
GTP
cGMP
↓[Ca^{2+}]
4 Na^+
6 Continued efflux of Ca^{2+} through the Na^+-Ca^{2+} exchanger reduces cytosolic [Ca^{2+}].
Plasma membrane
8 Rhodopsin kinase (RK) phosphorylates “bleached” rhodopsin; low [Ca^{2+}] and recoverin (Recov) stimulate this reaction. Arrestin (Arr) binds phosphorylated carboxyl terminus, inactivating rhodopsin.
9 Slowly, arrestin dissociates, rhodopsin is dephosphorylated, and all-*trans*-retinal is replaced with 11-*cis*-retinal. Rhodopsin is ready for another phototransduction cycle.
7 Reduction of [Ca^{2+}] activates guanylyl cyclase (GC) and inhibits PDE; [cGMP] rises toward “dark” level, reopening cation channels and returning V_m to prestimulus level.

❖Vitamin A is required for maintenance of epithelial cells, which form protective linings on many of the body’s organs.

❖The respiratory, gastrointestinal, and urogenital tracts, as well as the eye, are protected from environmental influences by mucous membranes.

❖If, however, there is a deficiency of vitamin A, epithelial cells that make up the membrane will change their characteristic structure.

❖It is postulated that vitamin A plays an important role in altering permeability of lipoprotein membranes of cells and of intracellular particles.

❖Vitamin A penetrates lipoprotein membranes and, at optimum levels, may act as a cross-linkage agent between the lipid and protein, thus stabilizing the membrane.

❖Animals deficient in vitamin A will show increased frequency and severity of bacterial, protozoal, and viral infections as well as other disease conditions.

❖Part of disease resistance, as a function of vitamin A, is related to maintenance of mucous membranes and normal functioning of the adrenal gland for production of corticosteroids needed to combat disease.

❖Vitamin A deficiency affects immune function, particularly the antibody response to T-cell–dependent antigens.

❖The absence of vitamin A in the ration will dramatically reduce reproductive ability.

❖In a number of species, vitamin A deficiency in the male results in a decline in sexual activity and failure of spermatogenesis, and in the female results in the resorption of the fetus, abortion, or birth of dead offspring.

❖In a number of species, vitamin A deficiency in the male results in a decline in sexual activity and failure of spermatogenesis, and in the female results in the resorption of the fetus, abortion, or birth of dead offspring.

❖Vitamin A has a role in the normal development of bone through control exercised over the activity of osteoclasts of the epithelial cartilage.

❖In vitamin A deficiency, osteoclast (reabsorbing bone) activity is reduced, resulting in excessive deposition of periosteal bone by the apparently unchecked function of osteoblasts (depositing bone).

❖Disorganized bone growth and irritation of the joints are two manifestations of vitamin A deficiencies.

❖Bone changes may also be responsible for the muscle incoordination and other nervous symptoms shown by vitamin A-deficient cattle, sheep, and swine.

❖These changes may be involved in the increase in cerebrospinal fluid pressure shown to be characteristic of the deficiency

❖Throughout history, night blindness and xerophthalmia have been the major signs of vitamin A deficiency in humans.

❖Xerophthalmia is the most common cause of blindness in young children throughout the world, with as many as 5 million Asian children developing xerophthalmia each year.

❖Vitamin A deficiency remains the second major nutritional problem among children in many countries, including Bangladesh, India, Indonesia, Brazil, and other developing countries.

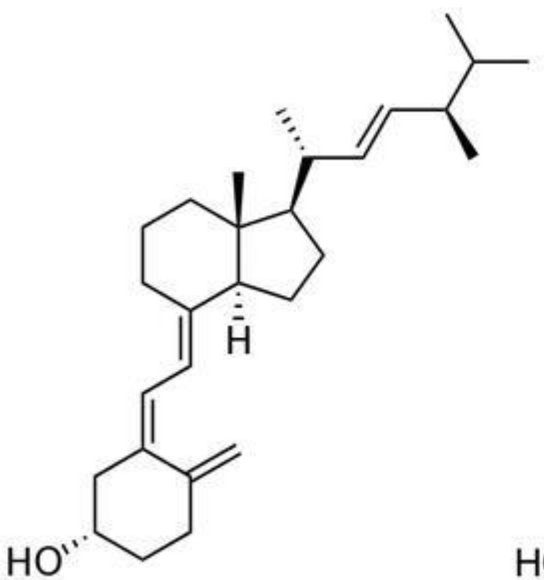
❖However, of all vitamins, vitamin A is most likely to be provided in toxic concentrations to both humans and livestock, and excess vitamin A has been demonstrated to have toxic effects in most species studied.

❖Large doses can be toxic, and many cases of overdoses have been reported in various species. The most characteristic signs of hypervitaminosis A are skeletal malformations, spontaneous fractures, and internal hemorrhage

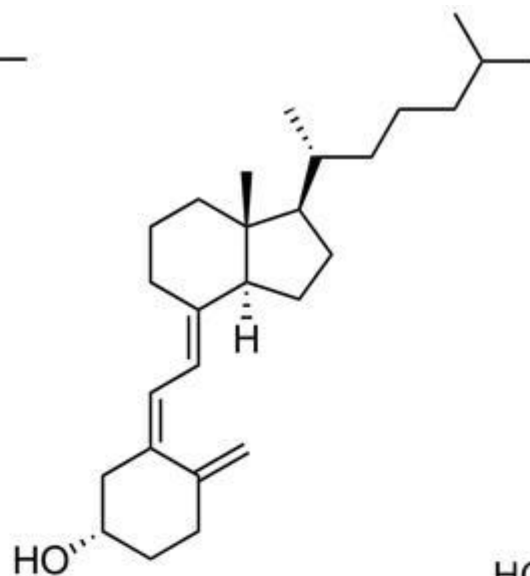
VITAMIN D

❖Vitamin D is thought of as the “sunshine vitamin” because it is synthesized by various materials when they are exposed to sufficient sunlight.

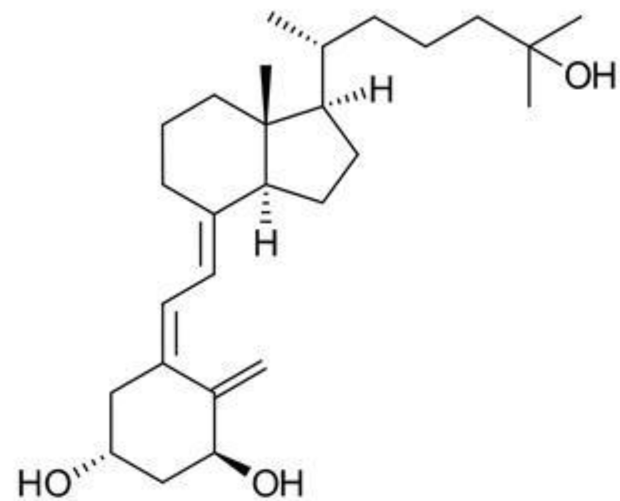
❖The two major natural sources of vitamin D are cholecalciferol (vitamin D3, which occurs in animals) and ergocalciferol (vitamin D2, which occurs predominantly in plants).



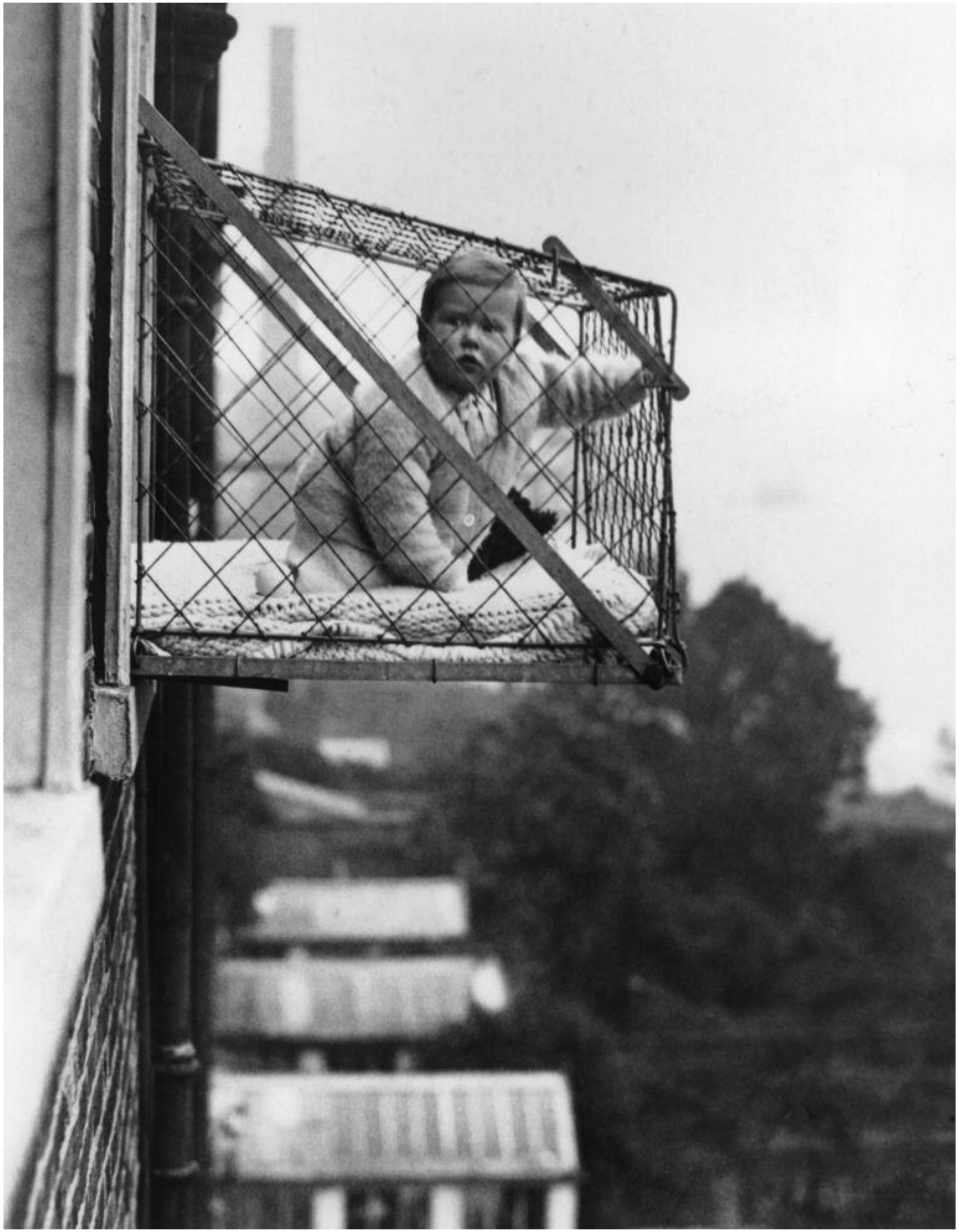
Vitamin D2 (Ergocalciferol)



Vitamin D3 (Cholecalciferol)



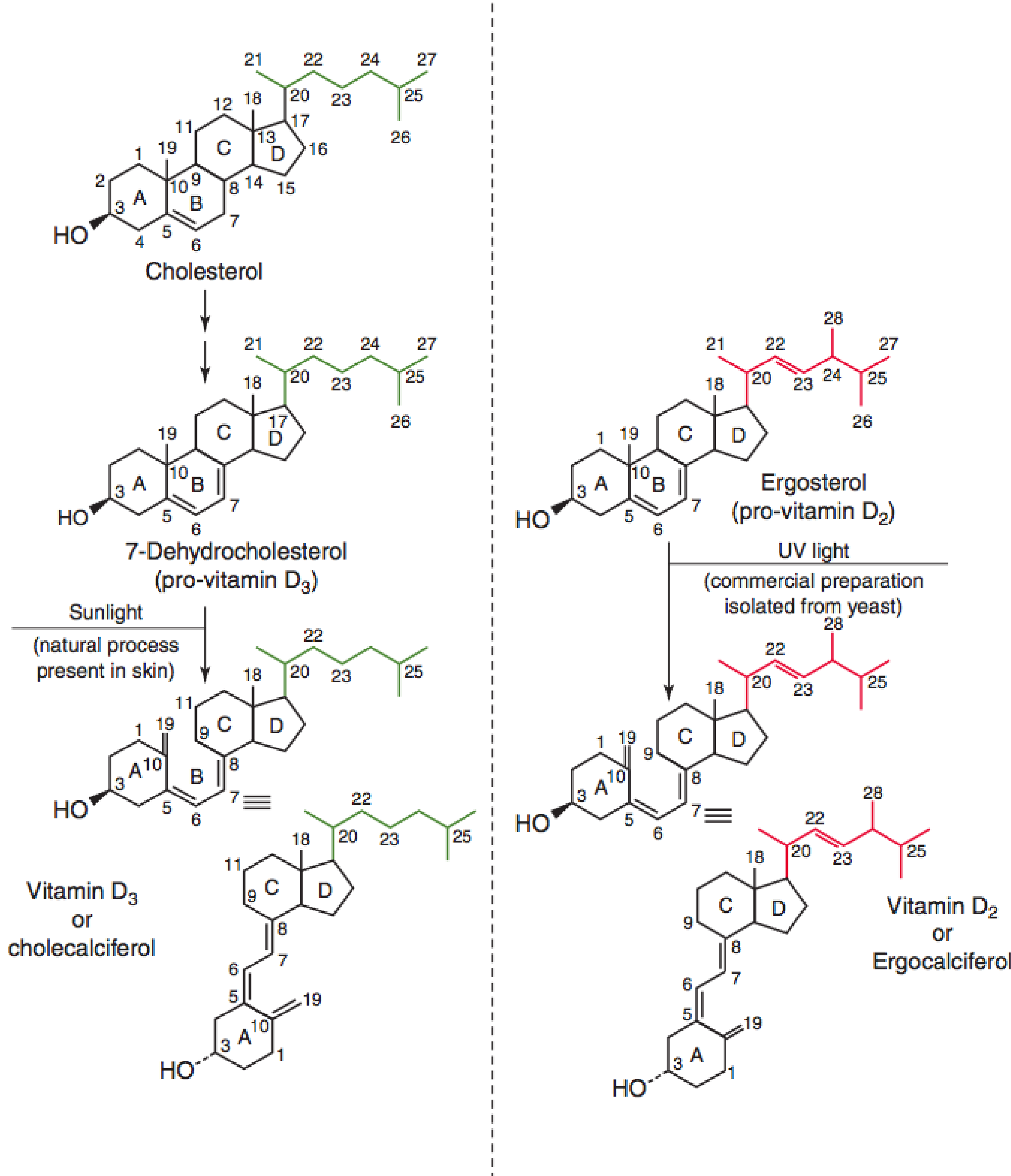
1,25-dihydroxycholecalciferol (Calcitriol)



❖Vitamin D designates a group of closely related compounds that possess antirachitic activity.

❖It may be supplied through the diet or by irradiation of the body. There are about 10 provitamins that, after irradiation, form compounds having variable antirachitic activity.

❖All sterols possessing vitamin D activity have the same steroid nucleus; they differ only in the nature of the side chain attached to carbon 17.



❖Ergocalciferol is derived from a common plant steroid, ergosterol, and is the usual dietary source of vitamin D.

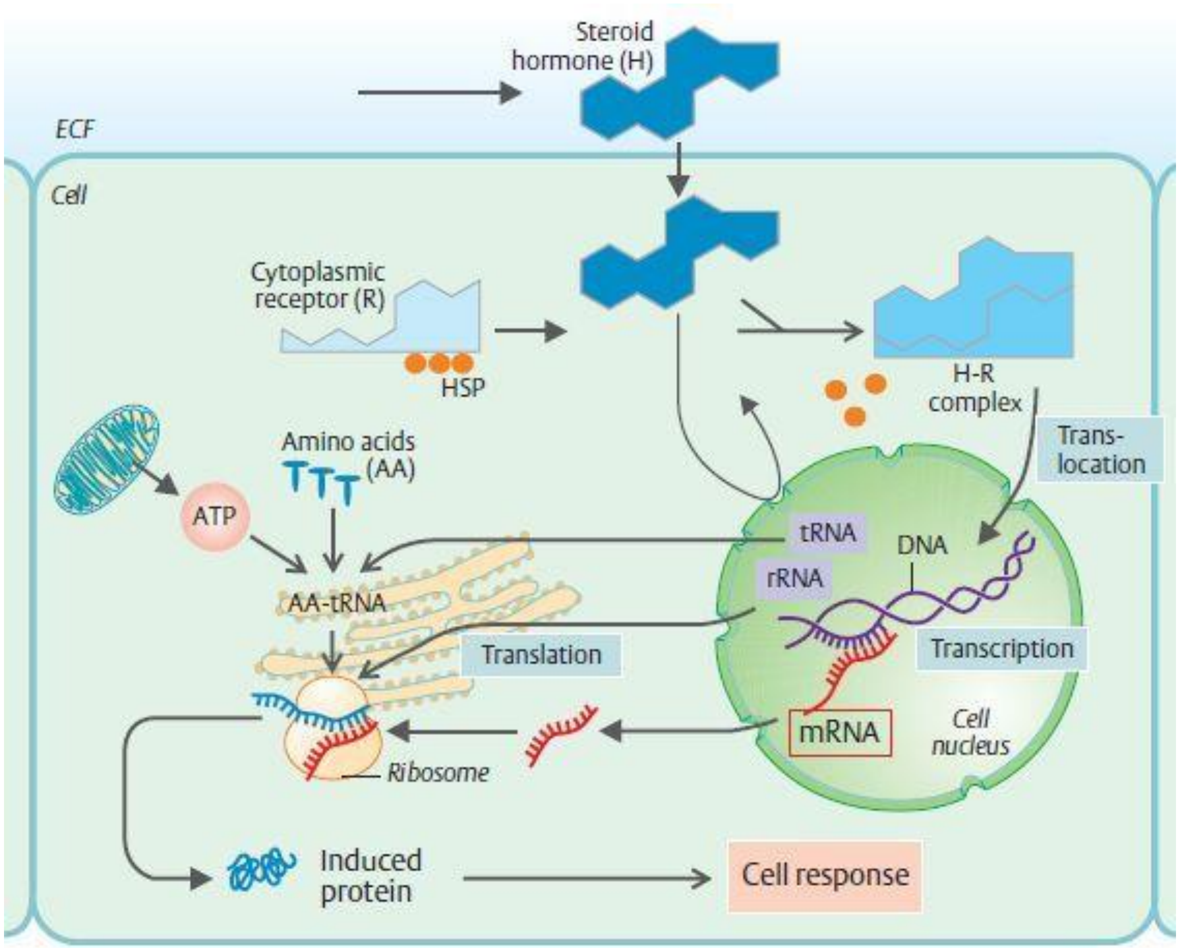
❖Cholecalciferol is produced exclusively from animal products. 7-Dehydrocholesterol is derived from cholesterol or squalene, which is synthesized in the body and present in large amounts in skin, intestinal wall, and other tissues.

❖Vitamin D precursors have no antirachitic activity until the B-ring is opened between the 9 and 10 positions by irradiation and a double bond is formed between carbons 10 and 19 to form vitamin D.

❖The general function of vitamin D is to elevate plasma Ca and P to a level that will support normal mineralization of bone as well as other body functions.

❖The active form of vitamin D, 1,25-$(OH)_2$D, functions as a steroid hormone.

❖The hormone is produced by an endocrine gland, circulated in blood bound to a carrier protein (DBP), and transported to target tissues.



❖Research suggests that 1,25-$(OH)_2$D3 may also generate biological responses via signal transduction mechanisms that are independent of the nuclear VDRs, which are termed nongenomic pathways.

❖Nongenomic responses can include stimulation of membrane lipid turnover, activation of Ca^{2+} channels, and elevation of intracellular Ca^{2+} concentrations.

❖Tetany in humans and animals results if plasma Ca levels are appreciably below normal. Two hormones—thyrocalcitonin (calcitonin) and parathyroid hormone (PTH)—function in a delicate relationship with 1,25-$(OH)_2$D to control blood Ca and P levels.

❖Vitamin D brings about an elevation of plasma Ca and P by stimulating specific pump mechanisms in the intestine, bone, and kidney.

❖These three sources of Ca and P thus provide reservoirs that enable vitamin D to elevate the levels of Ca and P in blood to levels that are necessary for normal bone mineralization and for other functions ascribed to Ca.

❖Vitamin D plays roles both in the mineralization of bone as well as demineralization or mobilization of bone mineral.

❖1,25-$(OH)_2D$ is one of the factors controlling the balance between bone formation and resorption.

❖During vitamin D deficiency, this organic matrix fails to mineralize, causing rickets in the young and osteomalacia in adults.

❖Vitamin D also plays a role in the mobilization of Ca from bone to the extracellular fluid compartment.

❖Another role of vitamin D has been proposed in addition to its involvement in bone; namely, in the biosynthesis of collagen in preparation for mineralization.

❖Vitamin D deficiency in children leads to the pathological bone condition called rickets, which is characterized by disordered cartilage cell growth and enlargement of the epiphyseal growth plates in the long bones

❖Although it is accepted that vitamin D is absolutely essential for growing children, it is not well appreciated that it is also essential for maintenance of a healthy mineralized skeleton in adults.

❖Excess consumption of vitamin D results in toxicity. After vitamin A, vitamin D is the vitamin most likely to be consumed in concentrations toxic to humans.

❖Excessive intake of vitamin D produces a variety of effects, all associated with abnormal elevation of blood Ca.

❖Elevated blood Ca is caused by greatly stimulated bone resorption, as well as increased intestinal Ca absorption.

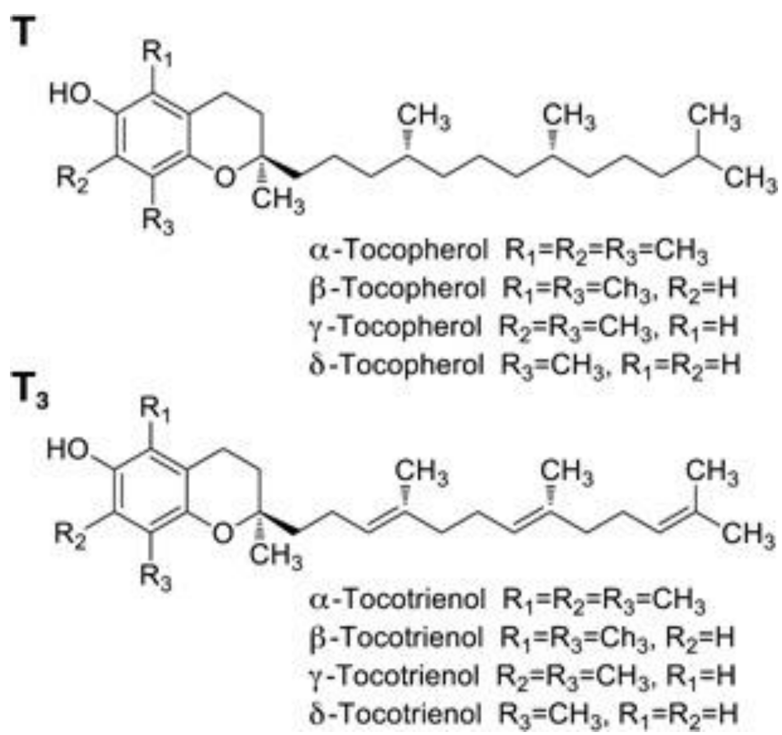
❖The main pathological effect of ingestion of massive doses of vitamin D is widespread calcification of soft tissues.

❖Other common observations of vitamin D toxicity are anorexia (loss of appetite), extensive weight loss, elevated blood Ca, and lowered blood phosphate.

VITAMIN E

❖Vitamin E is recognized as an essential nutrient for all species of animals, including humans.

❖Vitamin E has been shown to be important against free-radical injury; enhancing the immune response; and playing a role in prevention of cancer, heart disease, cataracts, Parkinson's disease, and a number of other disease conditions.



❖Vitamin E activity in food derives from a series of compounds of plant origin, the tocopherols and tocotrienols.

❖Eight forms of vitamin E are found in nature: four tocopherols (α, β, γ, and δ) and four tocotrienols (α, β, γ, and δ).

❖Vitamin E has been shown to be essential for integrity and optimum function of the reproductive, muscular, circulatory, nervous, and immune systems.

❖It is well established that some functions of vitamin E, however, can be fulfilled in part or entirely by traces of Se or by certain synthetic antioxidants.

❖Even the sulfur-bearing amino acids, cystine and methionine, affect certain vitamin E functions.

❖One of the most important functions is its role as an intercellular and intracellular antioxidant.

❖Vitamin E is part of the body's intracellular defense against the adverse effects of reactive oxygen and free radicals that initiate oxidation of unsaturated phospholipids and critical sulfhydryl groups. ,

❖Vitamin E functions as a quenching agent for free radical molecules with single, highly reactive electrons in their outer shells.

❖Free radicals can be extremely damaging to biological systems.

❖The antioxidant function of vitamin E is closely related to and synergistic with the role of Se.

❖Selenium has been shown to act in aqueous cell media (cytosol and mitochondrial matrix) by destroying hydrogen peroxide and hydroperoxides via the enzyme glutathione peroxidase (GSHpx) of which it is a co-factor.

❖α-Tocopherol may be involved in the formation of structural components of biological membranes, thus exerting a unique influence on architecture of membrane phospholipids.

❖Vitamin E is an inhibitor of platelet aggregation and may play a role by inhibiting peroxidation of arachidonic acid, which is required for formation of prostaglandins involved in platelet aggregation.

❖In addition to the relationship of vitamin E and Se, vitamin E, vitamin C, and β-carotene as antioxidant vitamins together have important tissue defense mechanisms against free-radical damage.

❖There is limited evidence that vitamin E is involved in biological oxidation-reduction reactions.

❖Vitamin E also appears to regulate the biosynthesis of DNA within cells.

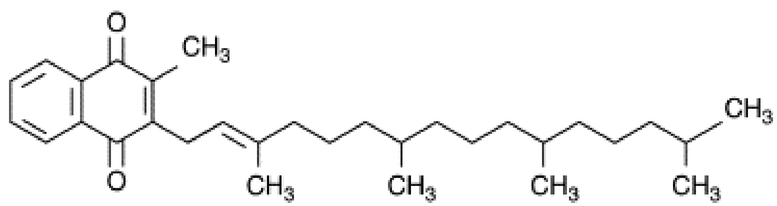
❖Muscular dystrophy seemed to be the one syndrome commonly encountered in vitamin E deficiency

VITAMIN K

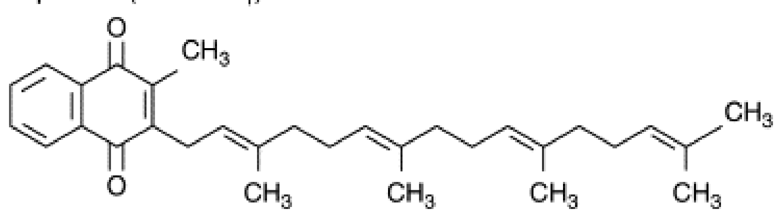
❖Vitamin K was the last fat-soluble vitamin to be discovered.

❖For many years after its discovery, vitamin K appeared to be limited in its function to only the normal blood-clotting mechanism.

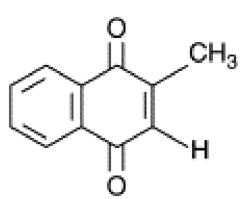
❖However, vitamin K-dependent proteins have been identified that suggest roles for the vitamin in addition to that of blood coagulation.



Phylloquinone (vitamin K_1)



Menaquinone-4 (vitamin K_2)



Menadione (vitamin K_3)

❖The general term vitamin K is now used to describe not a single chemical entity but a group of quinone compounds that have characteristic antihemorrhagic effects.

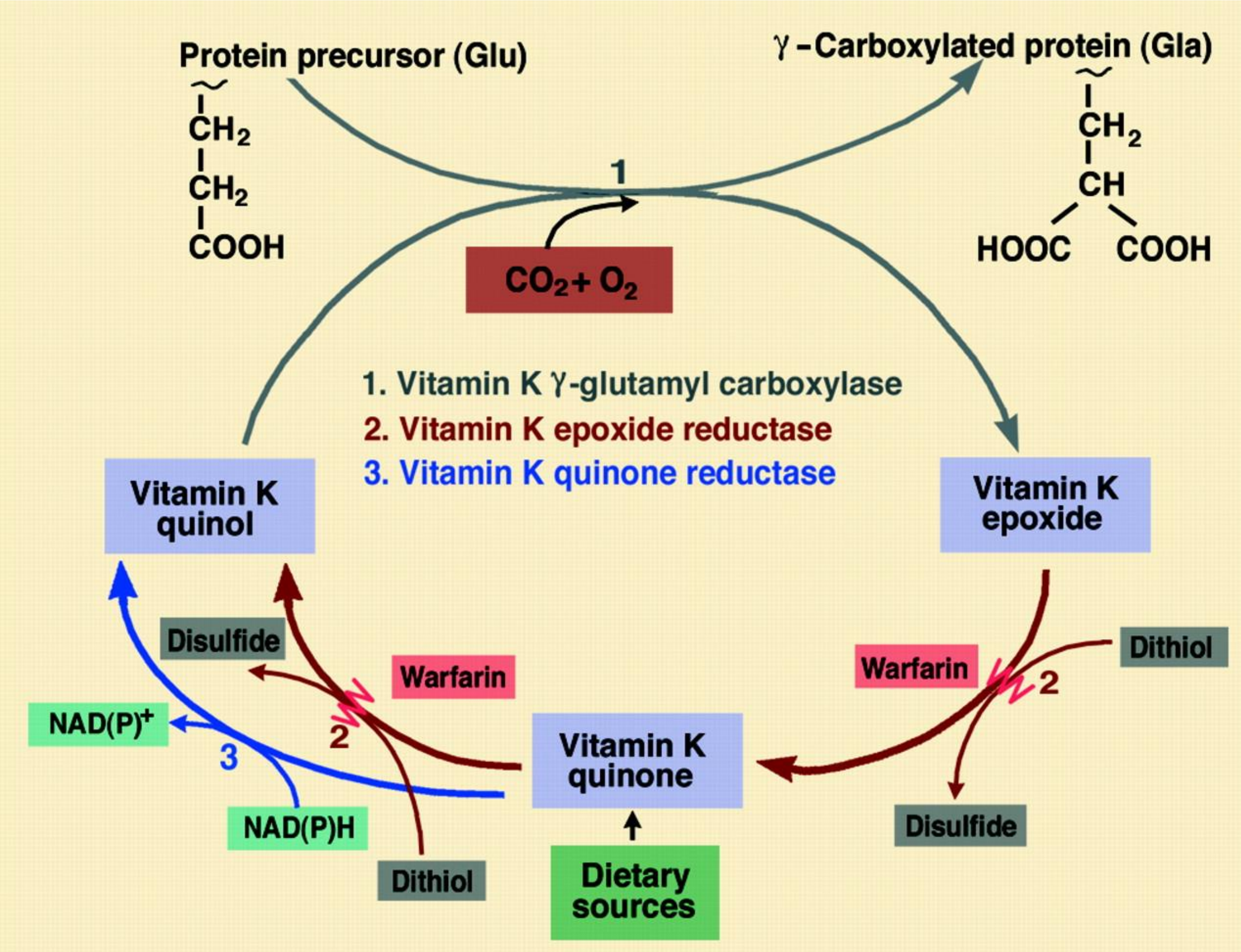
❖Vitamin K is a generic term for a homologous group of fat-soluble vitamins consisting of a 2-methyl-1,4-naphthoquinone, with the various isomers differing in the nature and length of the side chain.

❖Coagulation time of blood is the major function ascribed to vitamin K.

❖Four vitamin K-dependent proteins involved in blood coagulation were discovered early in the investigations of the vitamin as a result of hemorrhagic disease caused by deficiency.

❖The vitamin is required for the synthesis of the active form of prothrombin (factor II) and other plasma clotting factors (VII, IX, and X).

❖The metabolic function of vitamin K is as the coenzyme in the carboxylation of protein-incorporated glutamate residues.



Protein precursor (Glu)
CH2
CH2
COOH
γ-Carboxylated protein (Gla)
CH2
CH
HOOC
COOH
1
CO2 + O2
1. Vitamin K γ-glutamyl carboxylase
2. Vitamin K epoxide reductase
3. Vitamin K quinone reductase
Vitamin K quinol
Vitamin K epoxide
Disulfide
Warfarin
NAD(P)+
2
3
NAD(P)H
Dithiol
Vitamin K quinone
Dietary sources
Warfarin
Dithiol
2
Disulfide

❖Four other vitamin K-dependent proteins have been identified in plasma (C, S, Z, and M).

❖Proteins C and S play an anticoagulant rather than a procoagulant role in normal hemostasis.

❖Continuing research has revealed that vitamin K-dependent reactions are present in most tissues and not just blood, and that a reasonably large number of proteins are subjected to this posttranslational car boxylation of specific glutamate residues to γ-carboxyglutamate residues.

❖Vitamin K could be involved in the pathogenesis of bone mineral loss.

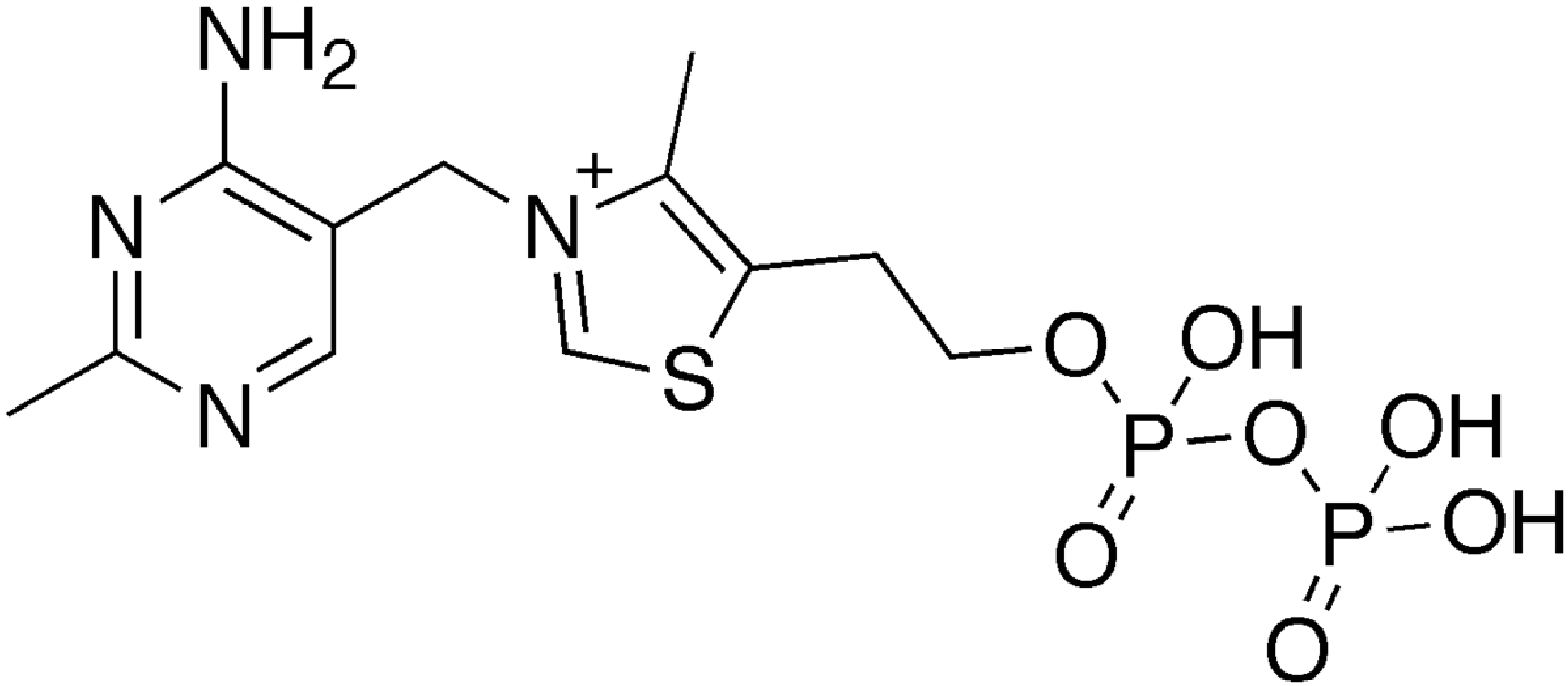
❖Vitamin K also has been suggested as a protective factor against gastric mucosal lesions, but the mechanism of protection is unclear.

❖The major clinical sign of vitamin K deficiency in all species is impairment of blood coagulation.

VITAMIN B1, THIAMIN

❖Thiamin (also called thiamine, aneurin[e], and vitamin B1) was the first vitamin to be discovered.

❖Thiamin consists of a molecule of pyrimidine and a molecule of thiazole linked by a methylene bridge; it contains both nitrogen and sulfur atoms.



❖Thiamin in all cells functions principally as the coenzyme cocarboxylase or TPP.

❖The citric acid cycle (Krebs cycle or tricarboxylic acid cycle) is responsible for production of energy in the body. In this cycle, breakdown products of carbohydrates, fats, and proteins are brought together for further breakdown and for synthesis.

❖The vitamins riboflavin, niacin, and pantothenic acid, as well as thiamin, play roles in the cycle.

❖Thiamin is the coenzyme for all enzymatic decarboxylations of α-keto acids.

❖Thus it functions in the oxidative decarboxylation of pyruvate to acetate, which in turn is combined with coenzyme A for entrance into the tricarboxylic cycle.

❖In mammals, thiamin is essential in two oxidative decarboxylation reactions in the citric acid cycle that take place in cell mitochondria and one reaction in the cytoplasm.

❖These are essential reactions for utilization of carbohydrates to provide energy.

❖Decarboxylation in the citric acid cycle removes carbon dioxide, and the substrate is converted into the compound having the next lower number of carbon atoms.

❖In the mitochondria, reactions pyruvate dehydrogenase forms acetyl CoA from pyruvate and α-ketoglutarate dehydrogenase to convert α-ketoglutarate to succinyl CoA.

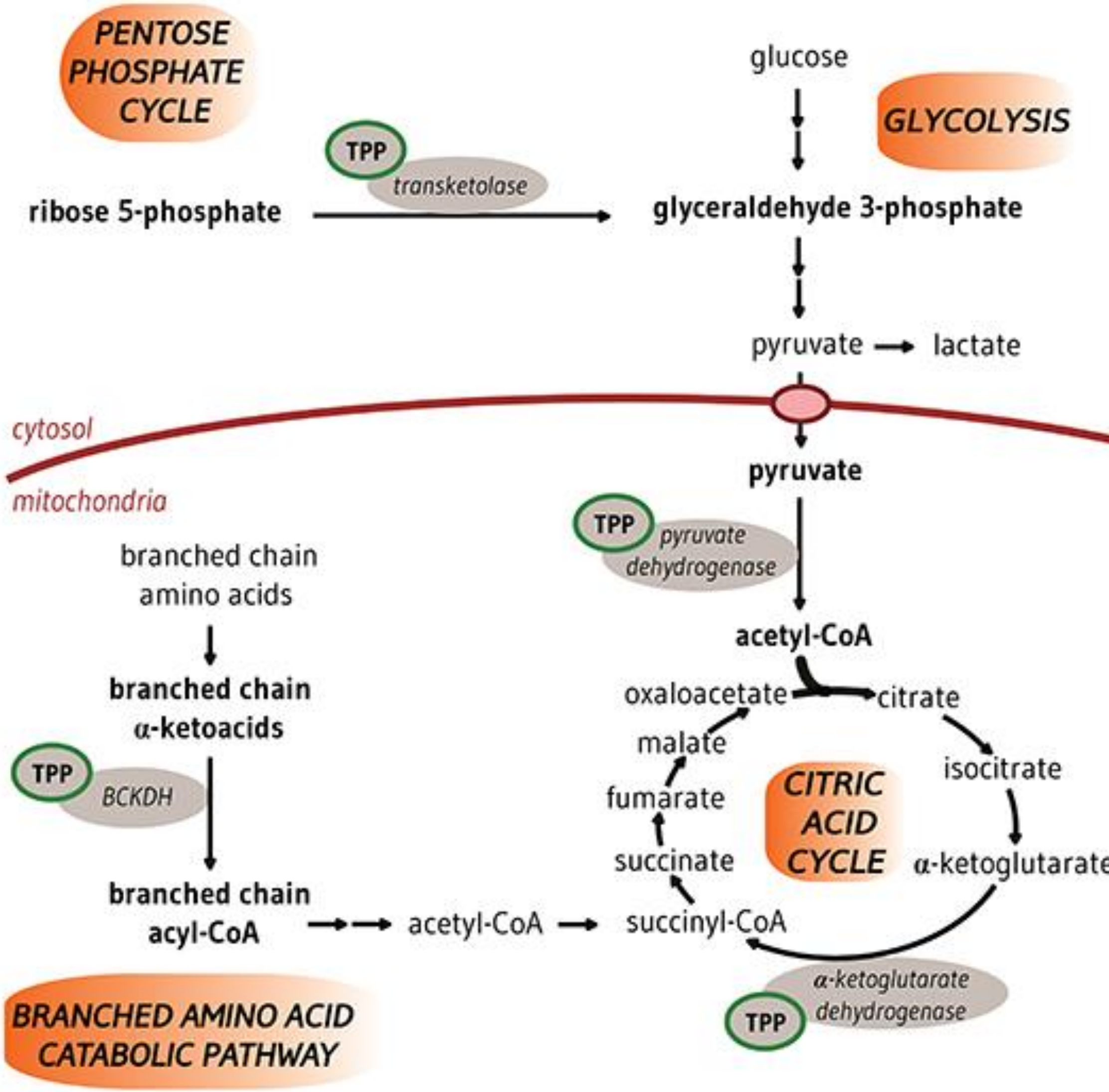
❖TPP is a coenzyme in the transketolase reaction that is part of the direction oxidative pathway (pentose phosphate cycle) of glucose metabolism that occurs not in mitochondria but in the cell cytoplasm in liver, brain, adrenal cortex, and kidney, but not skeletal muscle.

❖Thiamin has a vital role in nerve function, although the mechanism of action is unclear.

❖It has been postulated that thiamin, probably as TPP, plays an essential role in nerve transmission, apart from its enzymatic role in the Krebs cycle and the pentose pathway.

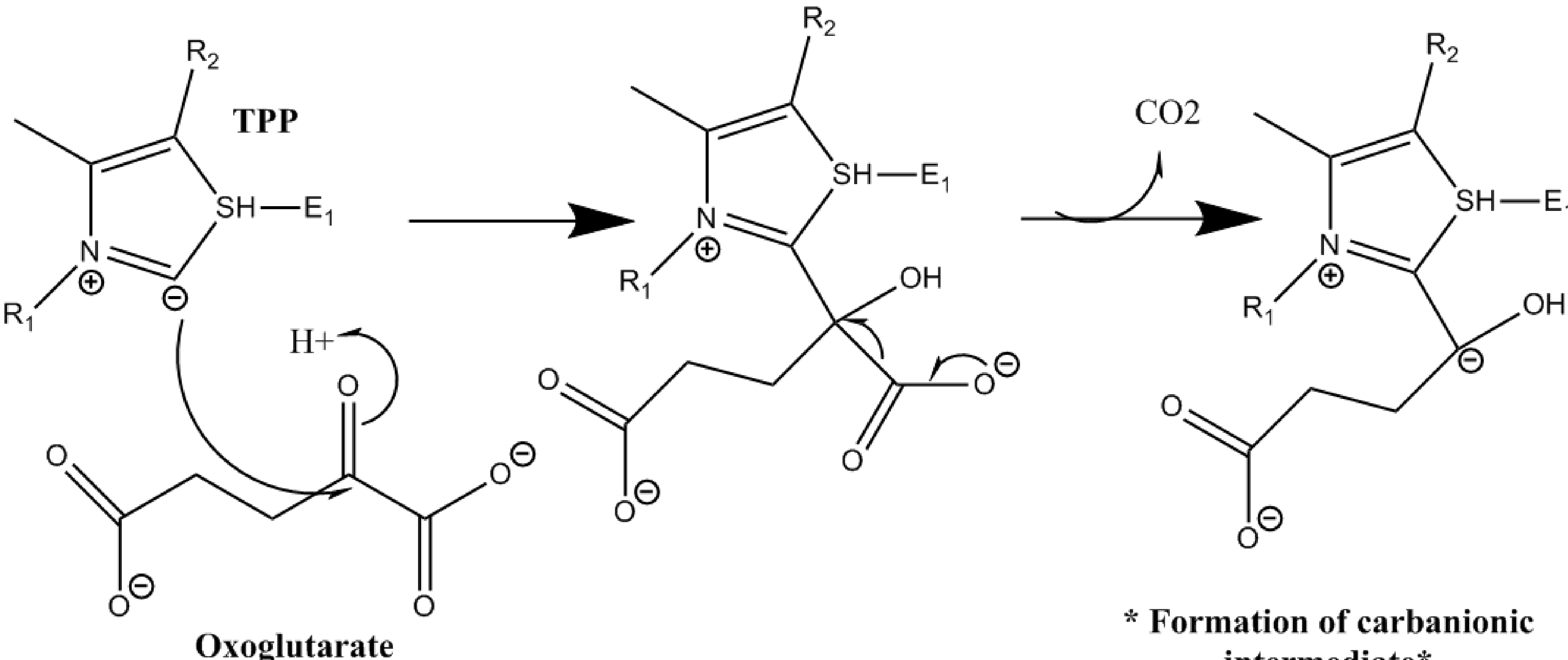
❖Thiamin has been shown to have a role in insulin biosynthesis. Isolated pancreatic islets from thiamin-deficient rats secreted less insulin than those from controls

Figure 1. Metabolic Pathways Requiring Thiamin Pyrophosphate



BCKDH, branched chain α-ketoacid dehydrogenase complex; CoA, coenzyme A; TPP, thiamin pyrophosphate.

Oxoglutarate Dehydrogenase E1-TPP Mechanism



*** Formation of carbanionic intermediate***

❖Thiamin has a vital role in nerve function, although the mechanism of action is unclear.

❖It has been postulated that thiamin, probably as TPP, plays an essential role in nerve transmission, apart from its enzymatic role in the Krebs cycle and the pentose pathway.

❖Thiamin has been shown to have a role in insulin biosynthesis. Isolated pancreatic islets from thiamin-deficient rats secreted less insulin than those from controls.

❖The classic diseases, beriberi in humans and polyneuritis in birds, represent a late stage of thiamin deficiency resulting from peripheral neuritis, perhaps caused by accumulation of intermediates of carbohydrate metabolism.

❖Disorders affecting the CNS are the same in all species. This is explained by the fact that in all animals, the brain covers its energy requirement chiefly by the degradation of glucose and is therefore dependent on biochemical reactions in which thiamin plays a key role.

❖In addition to neurological disorders, the other main group of disorders involves cardiovascular damage.

❖Clinical signs associated with heart function are slowing of heartbeat (bradycardia), enlargement of the heart, and edema. Less specific clinical signs include gastrointestinal problems, muscle weakness, easy fatigue, hyperirritability, and lack of appetite (anorexia).

❖Of all nutrients, thiamin deficiency has the most marked effect on appetite.

❖Animals consuming a low-thiamin diet soon show severe anorexia, lose all interest in food, and will not resume eating unless given thiamin.

❖Classic beriberi has been known since the earliest recorded times in the Far East, where it is endemic because of prevalent consumption of polished rice.

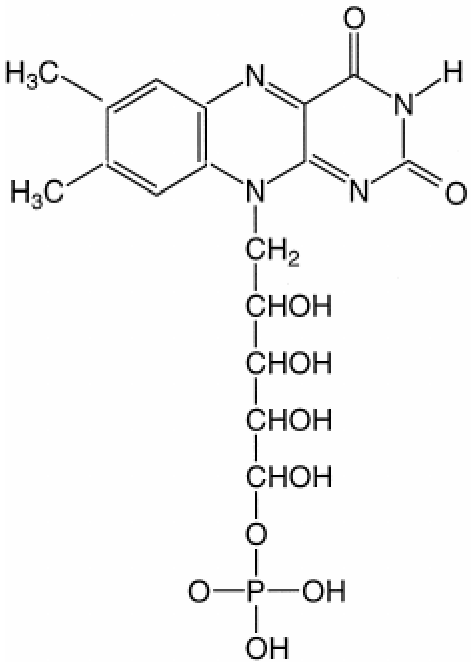
❖In beriberi, both cardiac and nervous functions are usually disturbed.

VITAMIN B2, RIBOFLAVIN

❖After isolation of thiamin (vitamin B1) as the “vitamin B” factor that prevented beriberi and polyneuritis, riboflavin (vitamin B2) was the first growth factor to be characterized from the remaining B-complex vitamins.

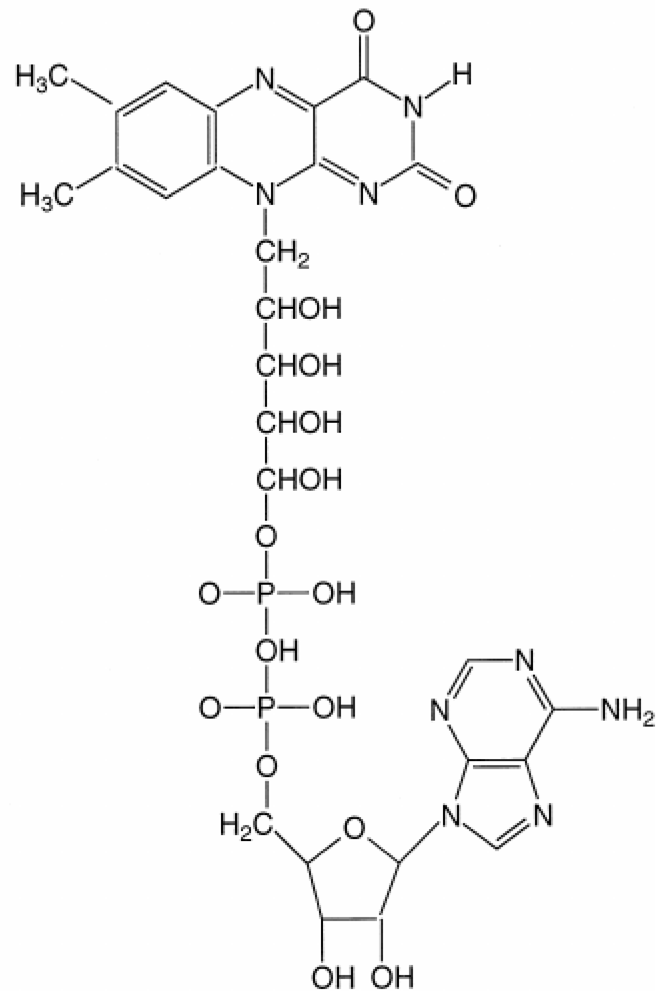
❖Riboflavin in the form of flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD) functions as a coenzyme in diverse enzymatic reactions.

FMN

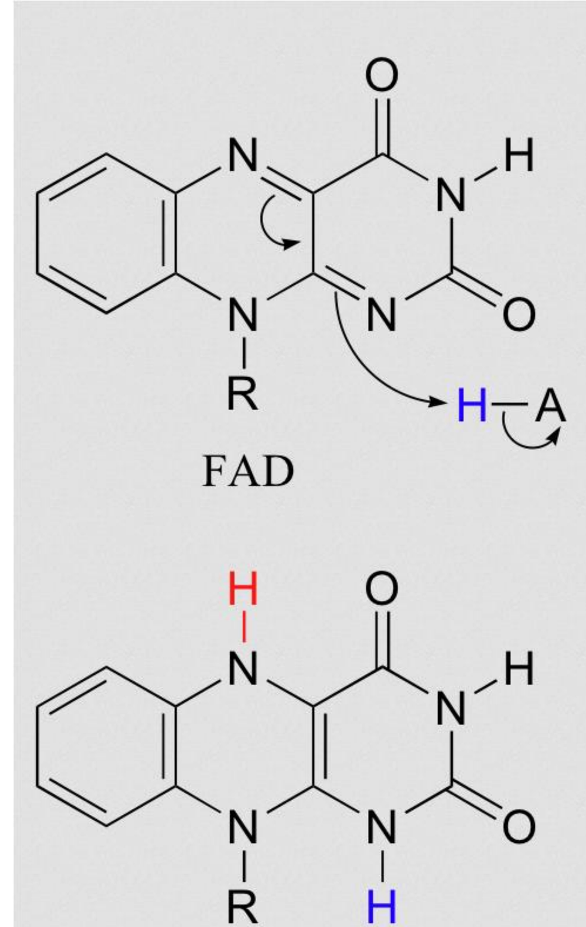


H3C
H3C
N
N
O
H
O
CH2
CHOH
CHOH
CHOH
CHOH
O
O—P—OH
OH

FAD



H3C
H3C
N
N
O
H
O
CH2
CHOH
CHOH
CHOH
CHOH
O
O—P—OH
OH
O—P—OH
O
H2C
O
N
NH2
OH OH



N
O
H
R
H—A
FAD

❖Riboflavin is required as part of many enzymes essential to utilization of carbohydrates, fat, and protein.

❖More than 100 enzymes are known to bind FAD or FMN in animal and microbial systems.

❖Riboflavin and related natural flavins participate in numerous and diverse reactions, perhaps more than for any other vitamin-coenzyme group.

❖FMN and FAD, which contain riboflavin, function as prosthetic groups that combine with specific proteins to form active enzymes called flavoproteins.

❖Riboflavin in these coenzyme forms acts as an intermediary in the transfer of electrons in biological oxidation-reduction reactions.

❖The enzymes that function aerobically are called oxidases, and those that function anaerobically are called dehydrogenases.

❖ By involvement in the hydrogen transport system, flavoproteins function by accepting and passing on hydrogen, undergoing alternate oxidation and reduction.

❖ The main function of FMN and FAD is transferring hydrogen between the niacin-containing coenzymes, NAD and NADP, the iron porphyrin cytochromes, and directly from the substrate.

❖ Riboflavin functions in flavoprotein-enzyme systems to help regulate cellular metabolism, and is also specifically involved in metabolism of carbohydrates.

❖ Since riboflavin plays many essential roles in the release of food energy and the assimilation of nutrients, it is understandable why deficiency is reflected in a wide variety of signs that vary among species.

❖ A decreased growth rate and lowered feed efficiency are common signs in all species affected.

VITAMIN B3, NIACIN

❖Niacin exerts its major physiological effects through its role in the enzyme system for cell respiration.

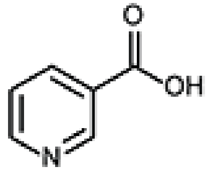
❖Niacin deficiency results in the disease pellagra in humans.

❖Chemically, niacin (C6H5O2N) is one of the simplest vitamins.

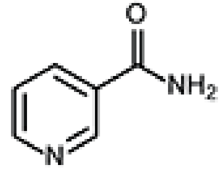
❖The two forms of niacin—nicotinic acid and nicotinamide—correspond to 3-pyridine carboxylic acid and its amide, respectively.

❖Nicotinic acid and nicotinamide (niacinamide) possess the same vitamin activity; the free acid is converted to the amide in the body.

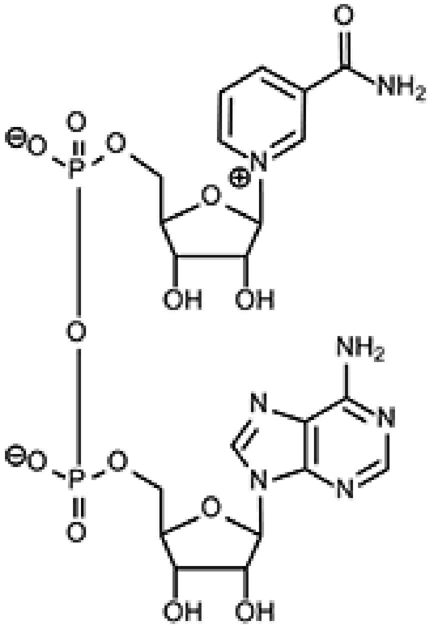
❖Nicotinamide functions as a component of two coenzymes: nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP)



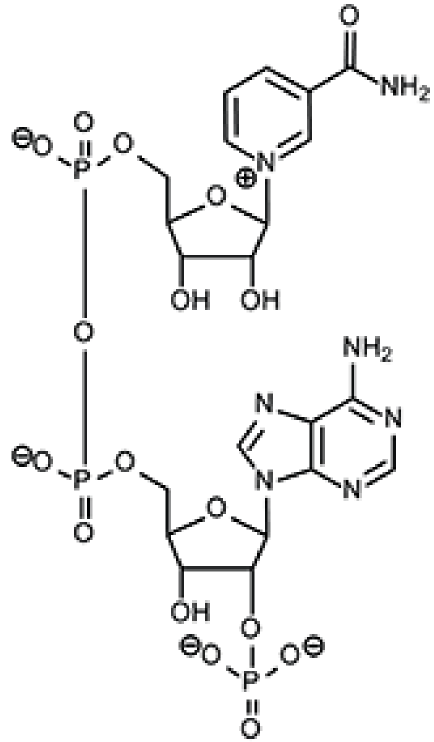
niacin
(nicotinic acid)



nicotinamide

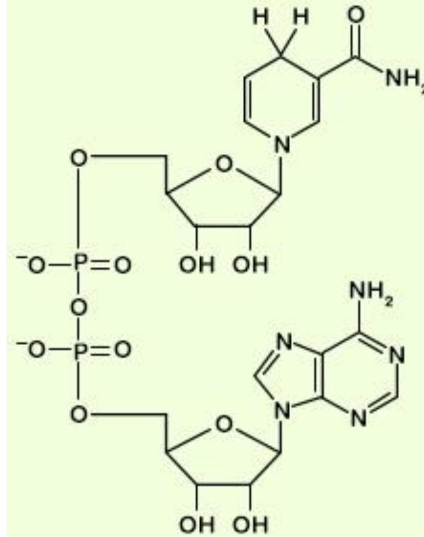


NAD

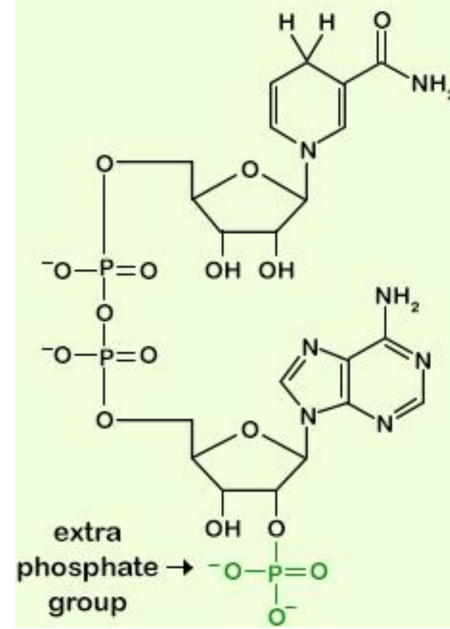


NADP

NADH



NADPH



❖The major function of niacin is in the coenzyme forms of nicotinamide, NAD and NADP. Enzymes containing NAD and NADP are important links in a series of reactions associated with carbohydrate, protein, and lipid metabolism.

❖They are especially important in the metabolic reactions that furnish energy to the animal.

❖The coenzymes act as an intermediate in most of the H+ transfers in metabolism, including more than 200 reactions in the metabolism of carbohydrates, fatty acids, and amino acids.

❖These reactions are of paramount importance for normal tissue integrity, particularly of the skin, gastrointestinal tract, and nervous system.

❖The NAD- and NADP-containing enzymes play an important role in biological oxidation-reduction systems by virtue of their capacity to serve as hydrogen-transfer agents.

❖Hydrogen is effectively transferred from the oxidizable substrate to oxygen through a series of graded enzymatic hydrogen transfers.

❖Nicotinamide-containing enzyme systems constitute one such group of hydrogen-transfer agents.

❖In electron transport, oxidation of reduced NAD or NADP is carried out by a second hydrogen-carrying system, the riboflavin coenzymes.

❖The nicotinamide moiety of the coenzyme operates in these systems by reversibly alternating between an oxidized quaternary pyridinium ion and a reduced tertiary amine. The transfer of hydrogen is reversible and stereospecific.

❖Some of these enzymes show a strict specificity for either NAD or NADP, while others utilize these coenzymes equally well.

❖Important metabolic reactions catalyzed by NAD and NADP are summarized below:

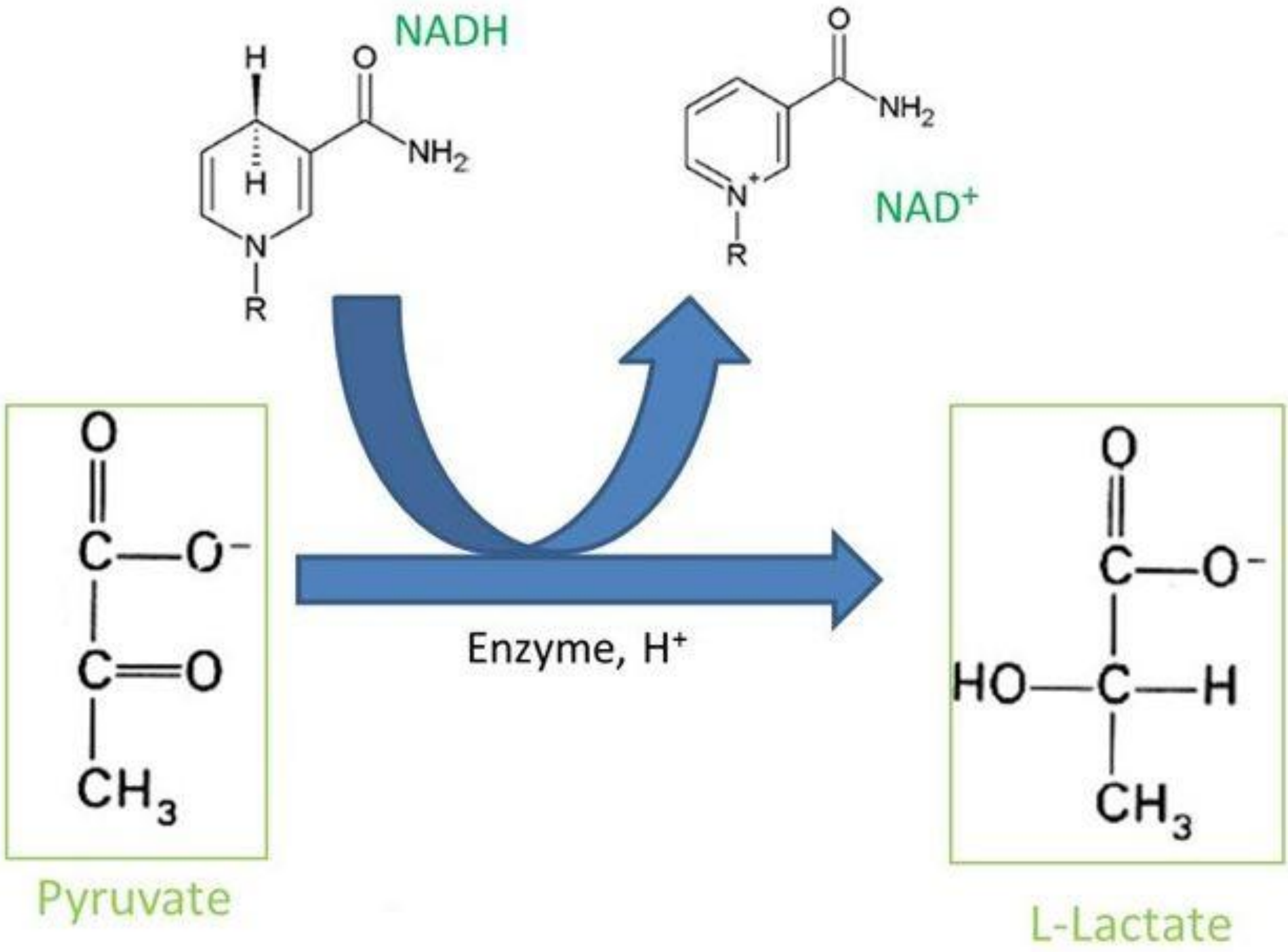
❖1. Carbohydrate metabolism—(a) glycolysis (anaerobic oxidation of glucose) and (b) the Krebs cycle.

❖2. Lipid metabolism—(a) glycerol synthesis and breakdown, (b) fatty acid oxidation and synthesis, and (c) steroid synthesis.

❖3. Protein metabolism—(a) degradation and synthesis of amino acids and (b) oxidation of carbon chains via the Krebs cycle.

❖4. Photosynthesis.

❖5. Rhodopsin synthesis


NADH
NAD+
Enzyme, H+
Pyruvate
L-Lactate

❖ Niacin deficiency is characterized by severe metabolic disorders in the skin and digestive organs.

❖ The first signs to appear are loss of appetite, retarded growth, weakness, digestive disorders, and diarrhea.

❖ The deficiency is found in both human and animal populations that are overly dependent on foods (particularly corn) low in available niacin and its precursor, tryptophan.

❖ Traditionally, niacin deficiency in humans has been equated with pellagra.

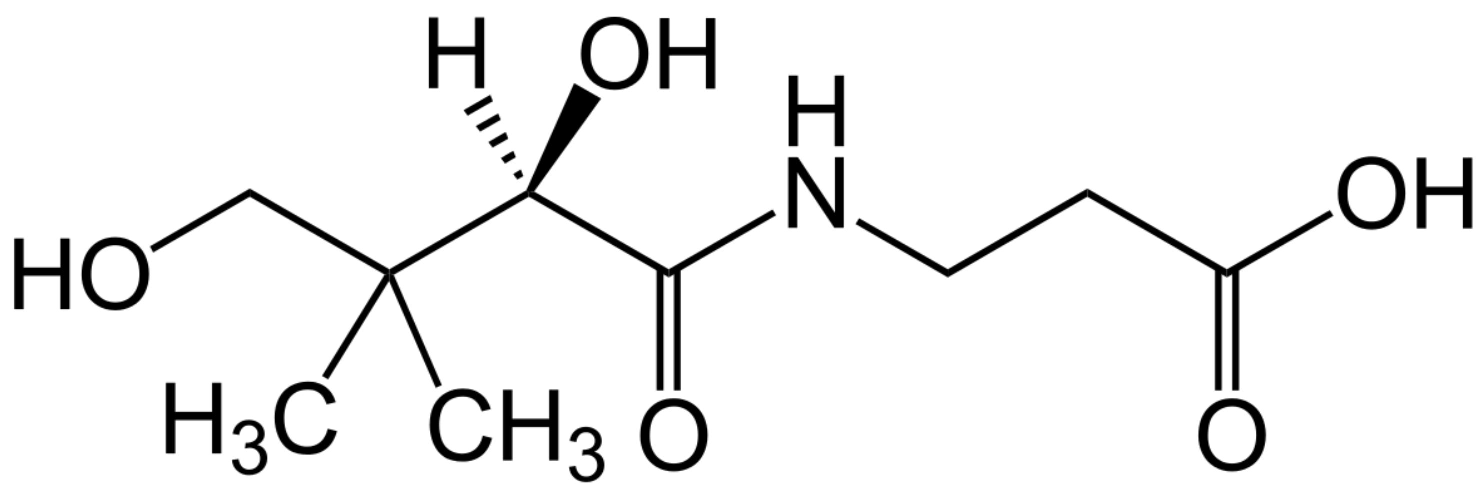
❖ Symptoms of deficiency can be considered under three headings: (1) skin changes; (2) lesions of the mucous membranes of the mouth, tongue, stomach, and intestinal tract; and (3) changes of nervous origin.

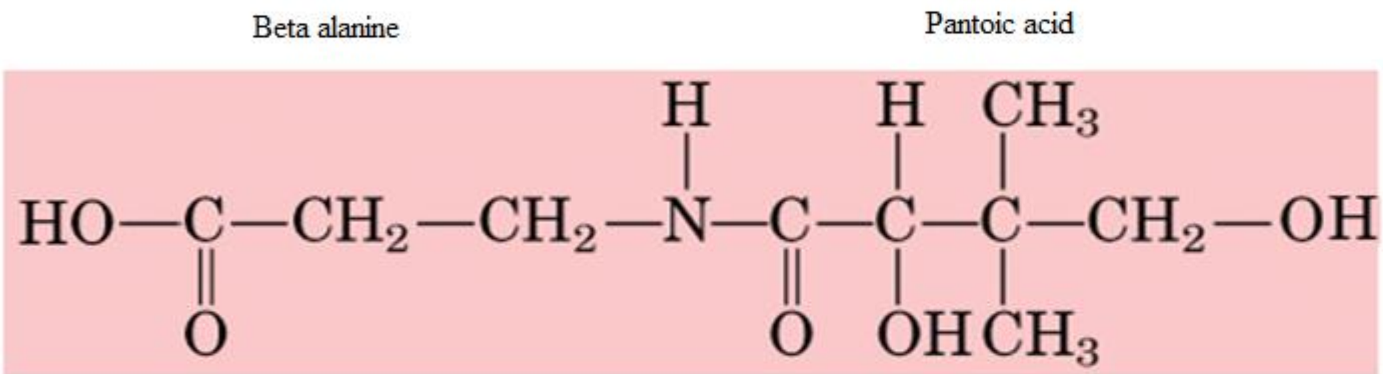
VITAMIN B5, PANTOTHENIC ACID

❖Two additional vitamins, pyridoxine (vitamin B6) and pantothenic acid, were found in the late 1930s as fractions of yeast and liver.

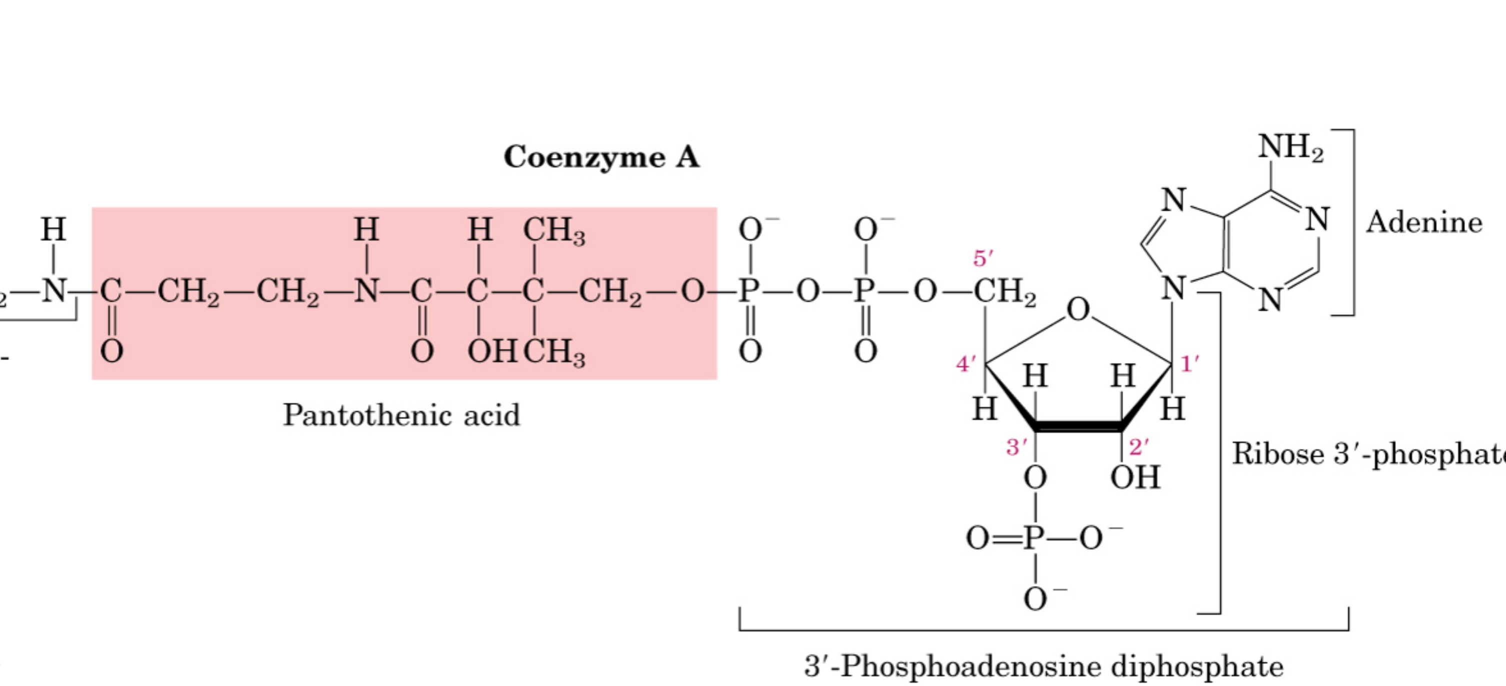
❖Tissue extracts from a variety of biological materials provided a growth factor for yeast that was identified as pantothenic acid, derived from the Greek word pantos, meaning “found everywhere.”

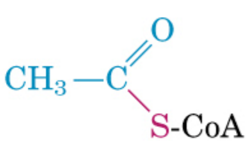
❖Pantothenic acid is found in two enzymes, coenzyme A and acyl carrier protein, which are involved in many reactions in carbohydrate, fat, and protein metabolism.





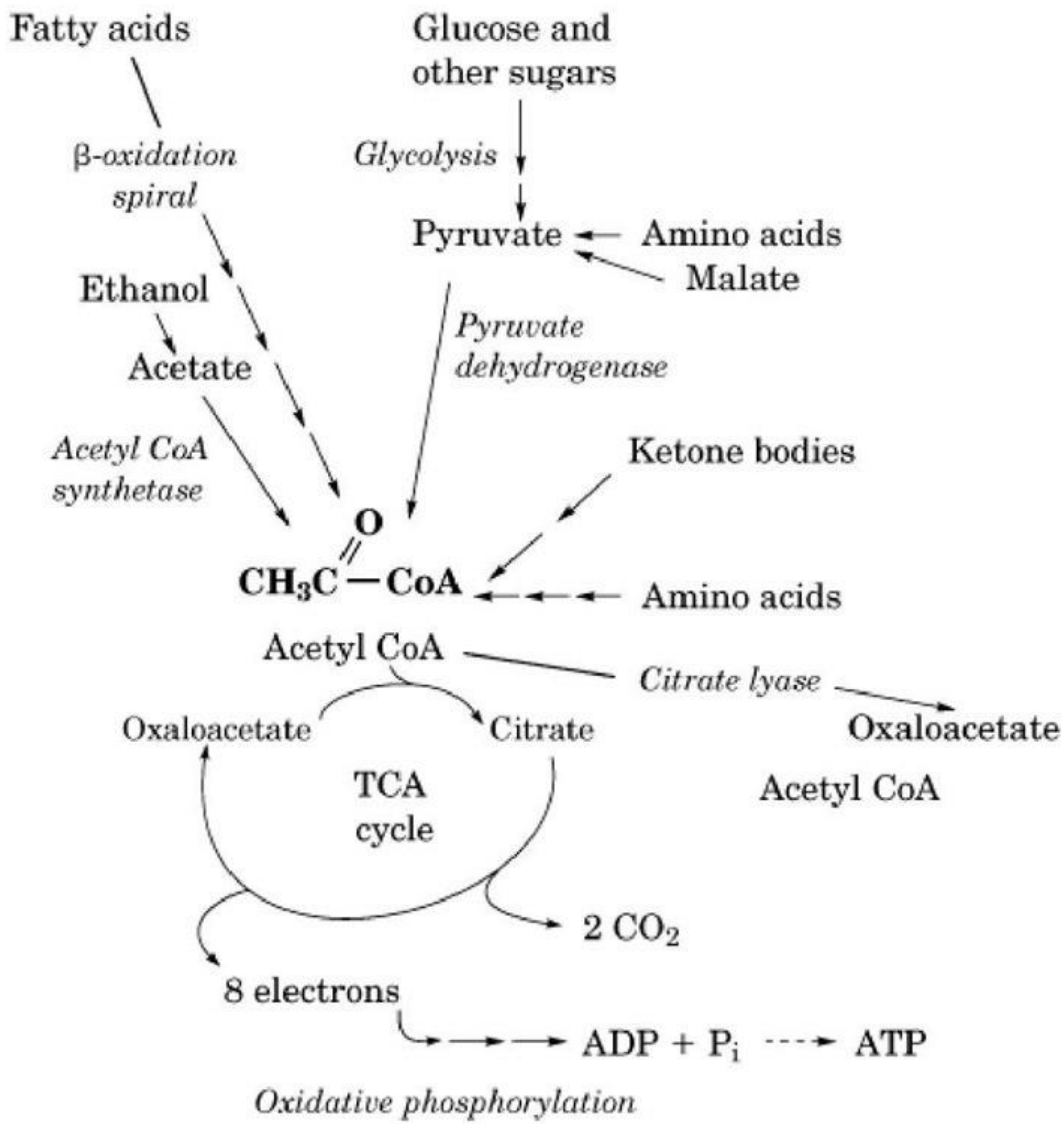
Pantothenic acid





Acetyl-CoA

❖Pantothenic acid functions as a constituent of two important coenzymes—coenzyme A and ACP. Coenzyme A is found in all tissues and is one of the most important coenzymes for tissue metabolism.



❖The most important function of coenzyme A is to act as a carrier mechanism for carboxylic acids.

❖Such acids, when bound to coenzyme A, have a high potential for transfer to other groups andare normally then referred to as “active.”

❖The most important of these reactions is the combination of coenzyme A with acetate to form “active acetate” with a high-energy bond that renders acetate capable of further chemical interactions.

❖As an example, it is utilized directly by combination with oxaloacetic acid to form citric acid, which enters the Krebs citric acid cycle.

❖Its combination with two-carbon fragments from fats, carbohydrates, and certain amino acids to form acetyl coenzyme A is an essential step in their complete metabolism, because the coenzyme enables these fragments to enter the citric acid cycle.

❖Coenzyme A functions as a carrier of acyl groups in enzymatic reactions involved in synthesis of fatty acids, cholesterol, and sterols; in the oxidation of fatty acids, pyruvate, and α-ketoglutarate; and in biological acetylations.

❖Coenzyme A has an essential function in lipid metabolism, fatty acids are activated by formation of the coenzyme derivative, and degradation by removal of acetate fragments in beta oxidation also uses another molecule of coenzyme A.

■ **Table 10.1 Selected Biochemical Reactions Catalyzed by Coenzyme A**

Enzyme	Pantothenate Derivative	Reactant	Product	Site
Pyruvic dehydrogenase	CoA	Pyruvate	Acetyl-CoA	Mitochondria
α-Ketoglutarate dehydrogenase	CoA	α-Ketoglutarate	Succinyl-CoA	Mitochondria
Fatty acid oxidase	CoA	Palmitate	Acetyl-CoA	Mitochondria
Fatty acid synthetase	Acyl carrier protein	Acetyl-CoA, Malonyl-CoA	Palmitate	Microsomes
Propionyl-CoA carboxylase	CoA	Propionyl-CoA, carbon dioxide	Methylmalonyl-CoA	Microsomes
Acyl-CoA synthetase	Phosphopantheteine	Succinyl-CoA, GDP + P_1	Succinate, GTP + CoA	Mitochondria

❖On the basis of observations on pantothenic acid-deficient animals and studies in human volunteers, deficiency of the vitamin is shown in the following signs and symptoms:

❖1. Reduced growth and feed conversion efficiency. 2. Lesions of skin and its appendages. 3. Disorders of the nervous system. 4. Gastrointestinal disturbances. 5. Inhibition of antibody formation and thus decreased resistance to infection. 6. Impairment of adrenal function.

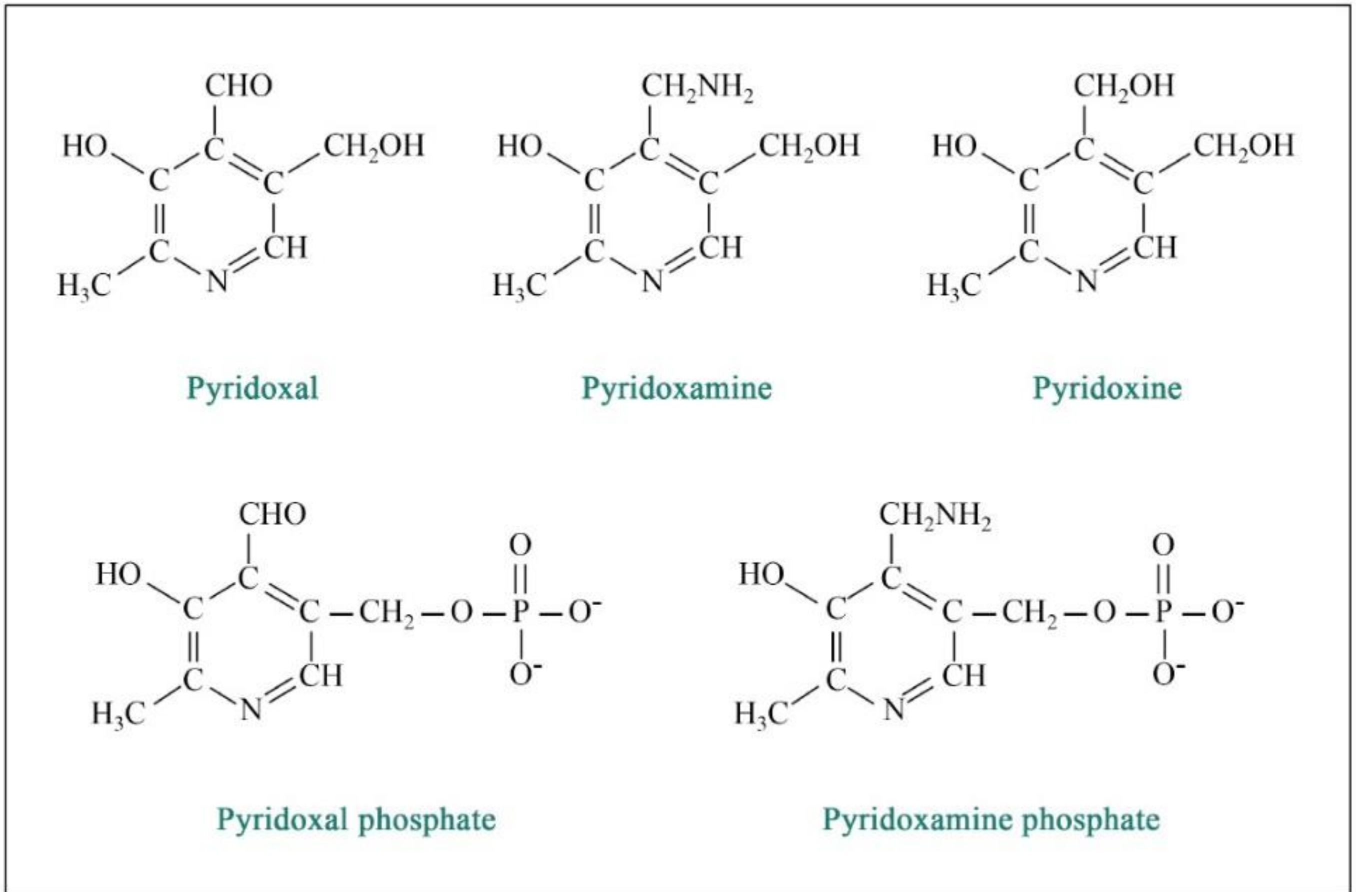
❖In humans, additional emotional and neurological symptoms include hyperventilation, irritability, insomnia, depression, headache, and dizziness.

❖Since pantothenic acid is so widely distributed in nature, clear-cut deficiency symptoms in humans are rarely found in practice except when associated with severe malnutrition.

VITAMIN B6, PYRIDOXAL PHOSPHATE

❖Vitamin B6 refers to a group of three compounds: pyridoxol (pyridoxine), pyridoxal, and pyridoxamine.

❖Vitamin B6 acts as a component of many enzymes that are involved in the metabolism of proteins, fats, and carbohydrates. The vitamin is particularly involved in various aspects of protein metabolism.



❖Vitamin B 6 is a relatively simple compound with three substituted pyridine derivatives that differ only in functional group in the 4-position: alcohol (pyridoxine or pyridoxol), aldehyde pyridoxal, and amine pyridoxamine.

❖Pyridoxine is the predominant form in plants, whereas pyridoxal and pyridoxamine are the forms generally found in animal products.

❖These three forms have equal activity when administered parenterally to animals.

❖Two additional vitamin B6 forms found in foods are the coenzyme forms of pyridoxal phosphate (PLP) and pyridoxamine phosphate.

❖Various forms of vitamin B6 found in animal tissues are interconvertible, with vitamin B6 metabolically active mainly as PLP and to a lesser degree as pyridoxamine phosphate.

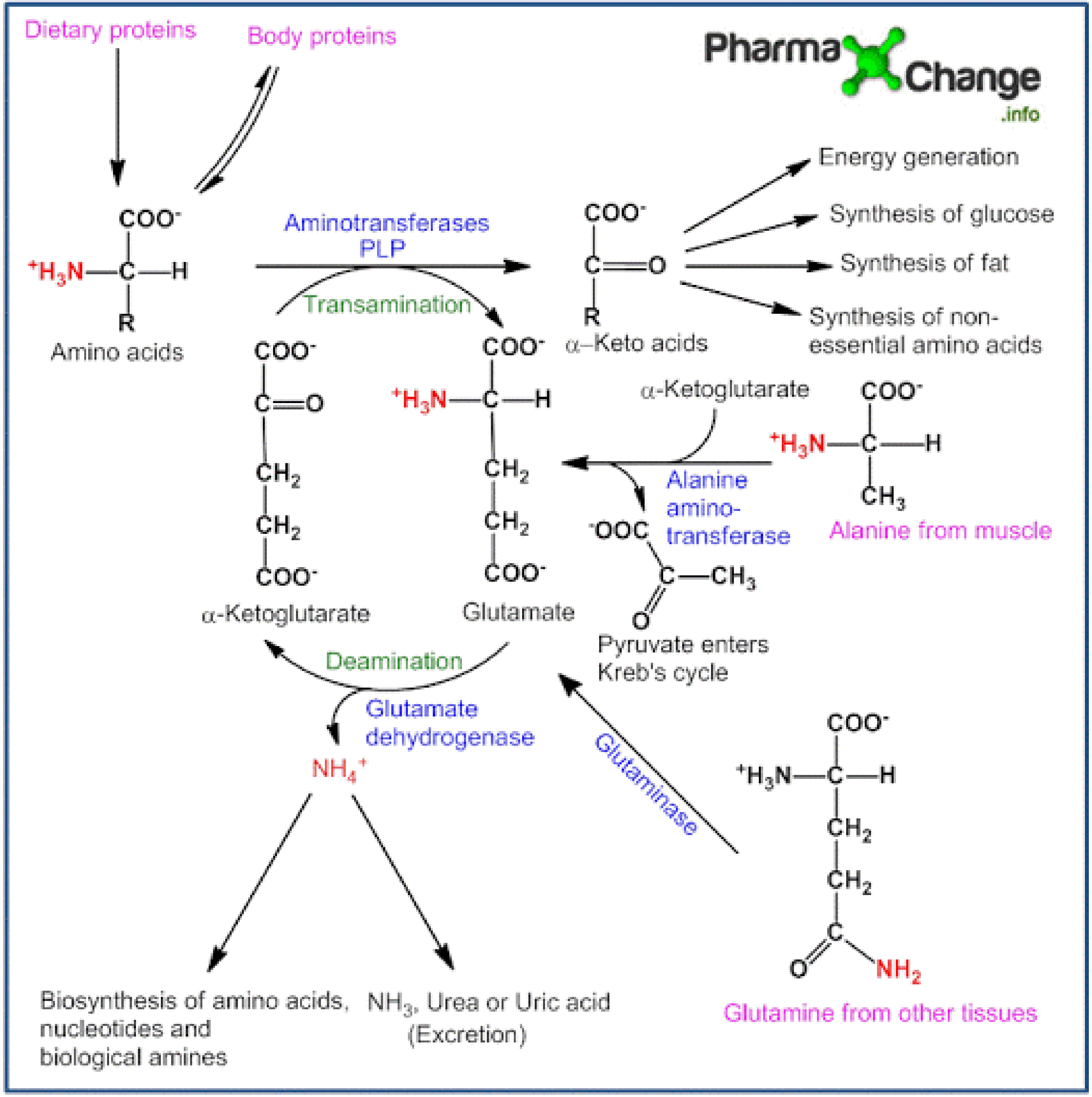
❖Vitamin B6 in the form of PLP (also named codecarboxylase), and to a lesser degree pyridoxamine phosphate, plays an essential role in the interaction of amino acid, carbohydrate, and fatty acid metabolism and the energy-producing citric acid cycle.

❖More than 60 enzymes are already known to depend on vitamin B6 coenzymes.

❖They typically bind the coenzyme tightly in a Schiff base linkage with the ε-amino group of an active-site lysine, and for most of the enzymes, the incoming substrate displaces the lysine to form a new Schiff base.

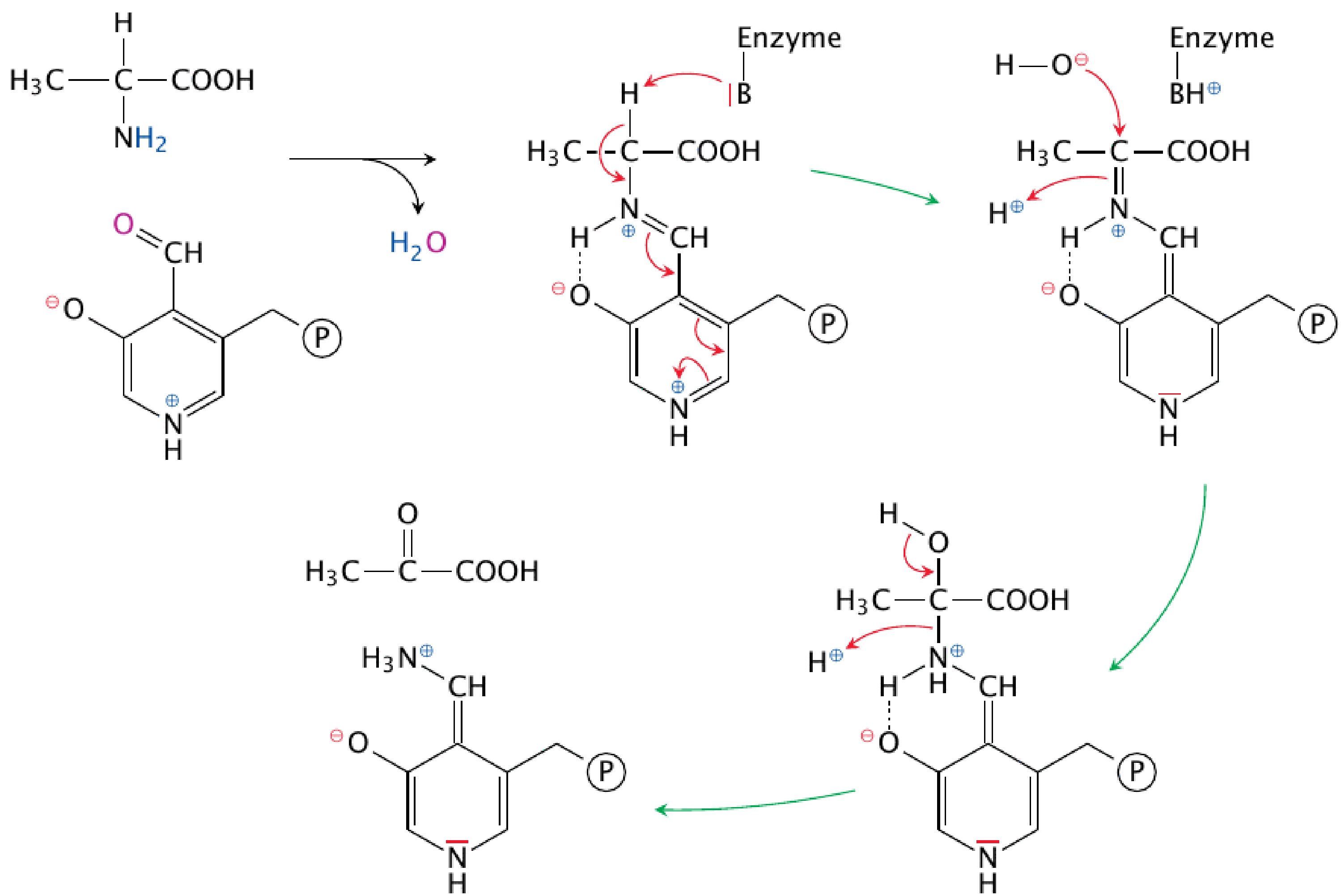
❖This results in a strong electron sink adjacent to several of the bonds on the substrate and facilitates a variety of chemical reactions.

❖Pyridoxal phosphate functions in practically all reactions involved in amino acid metabolism, including transamination (aminotransferase), decarboxylation, deamination, and desulfhydration, and in the cleavage or synthesis of amino acids.



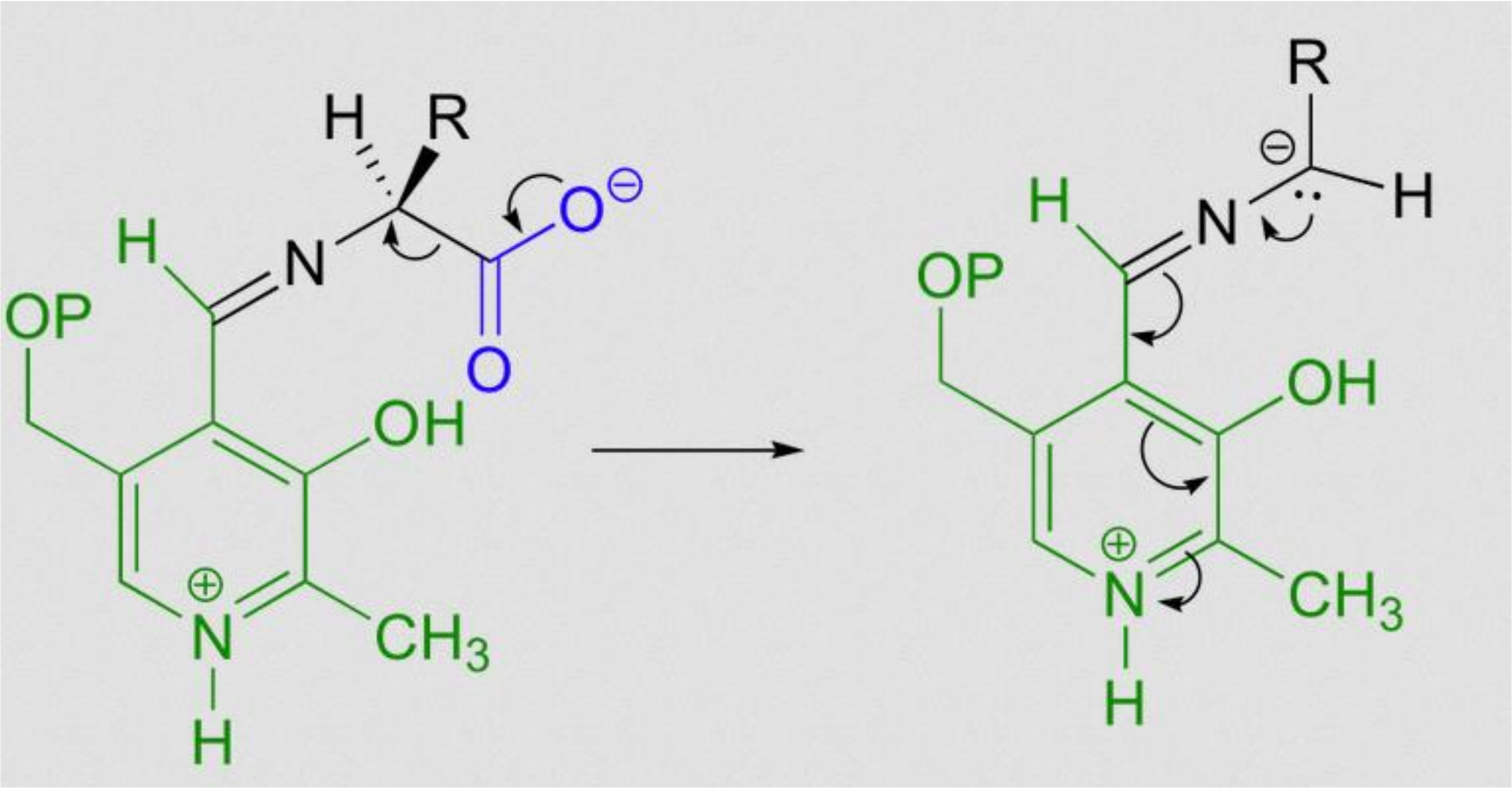
Dietary proteins
Body proteins
PharmaChange .info
COO⁻
⁺H₃N—C—H
R
Amino acids
Aminotransferases
PLP
Transamination
COO⁻
C=O
R
α–Keto acids
Energy generation
Synthesis of glucose
Synthesis of fat
Synthesis of non-essential amino acids
α-Ketoglutarate
Glutamate
α-Ketoglutarate
Alanine amino-transferase
Alanine from muscle
Pyruvate enters Kreb's cycle
Deamination
Glutamate dehydrogenase
NH₄⁺
Glutaminase
Glutamine from other tissues
Biosynthesis of amino acids, nucleotides and biological amines
NH₃, Urea or Uric acid (Excretion)

❖The largest group of the vitamin B6-dependent enzymes are the transaminases, most of which use α-ketoglutarates as the amino group acceptor.



❖Nonoxidative decarboxylation reactions also involve PLP as a coenzyme.

❖Decarboxylases convert amino acids to biogenic amines, such as histamine, hydroxytyramine, serotonin, γ-aminobutyric acid, ethanolamine, and taurine, some of which are substances of high physiological activity.



- ❖Animal and human studies suggest that vitamin B6 deficiency affects both humoral and cell-mediated immune responses.

- ❖In humans, vitamin B6 depletion significantly decreased percentage and total number of lymphocytes, mitogenic responses of peripheral blood lymphocytes to T- and B-cell mitogens, and interleukin 2 production.

- ❖Characteristics of vitamin B6 deficiency are retarded growth, dermatitis, epileptic-like convulsions, anemia, and partial alopecia.

- ❖A high proportion of the human population receives inadequate dietary vitamin B6, particularly young and pregnant or lactating women.

- ❖Typical vitamin B6 deficiency symptoms in humans include hypochromic, microcytic anemia, loss of weight, abdominal distress, vomiting, hyperirritability, epileptic-type convulsions in infants, depression and confusion followed by convulsions in adults, and electroencephalographic abnormalities.

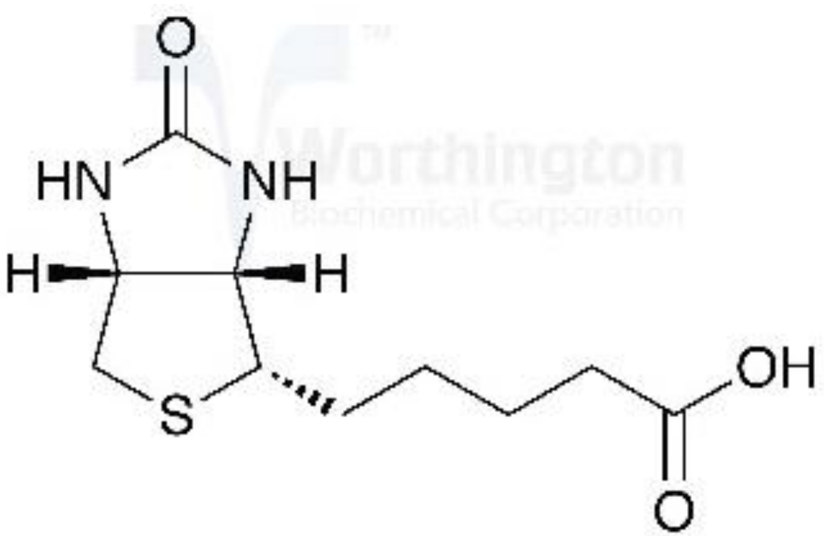
VITAMIN B7, BIOTIN

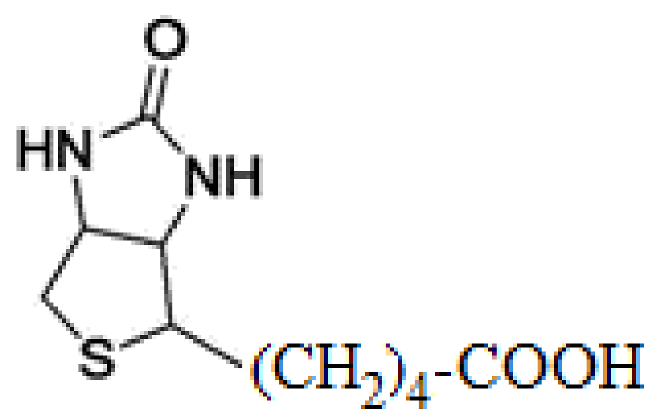
❖The chemical structure of biotin in metabolism includes a sulfur atom in its ring (like thiamin) and a transverse bond across the ring.

❖Biotin is a fusion of an imidazolidone ring with a tetrahydrothiophene ring bearing a valeric acid side chain.

❖Biotin, with its rather unique structure, contains three asymmetric carbonations, and therefore eight different isomers are possible.

❖Of these isomers only one contains vitamin activity, d-biotin.





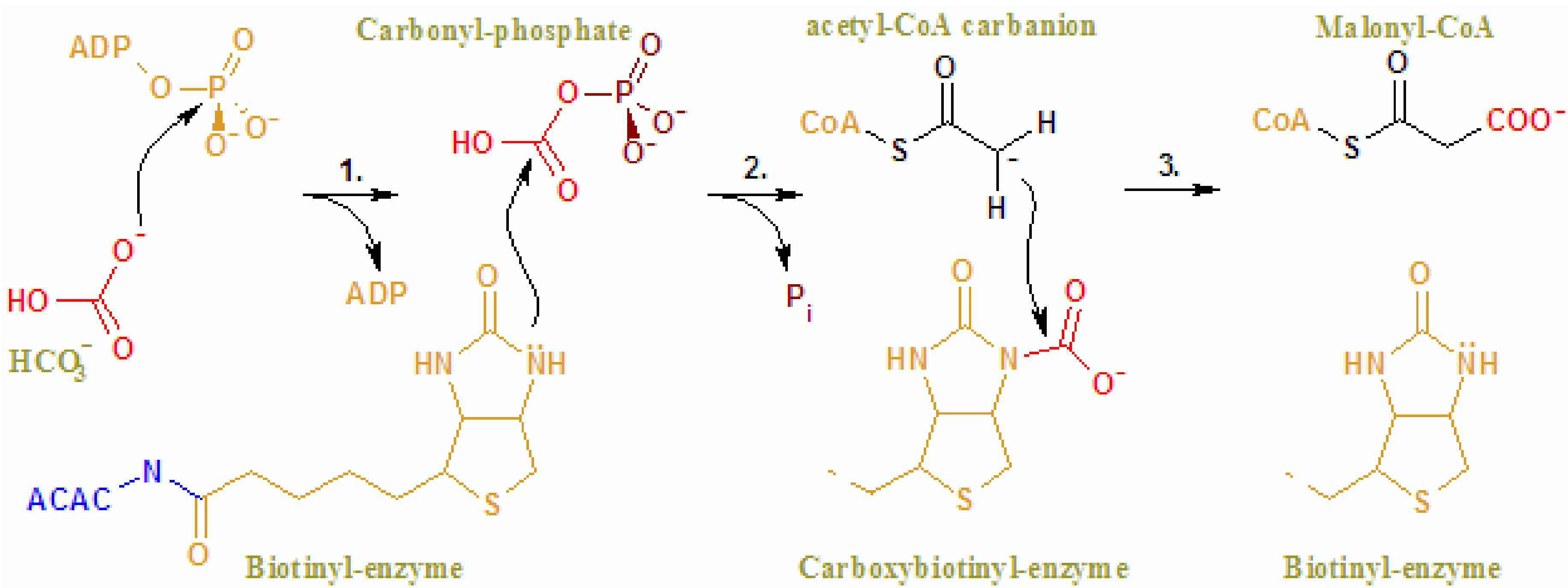
❖Biotin is an essential coenzyme in carbohydrate, fat, and protein metabolism. It is involved in conversion of carbohydrate to protein and vice versa as well as conversion of protein and carbohydrate to fat.

❖Biotin also plays an important role in maintaining normal blood glucose levels from metabolism of protein and fat when dietary intake of carbohydrate is low.

❖Biotin serves as a prosthetic group in a number of enzymes in which the biotin moiety functions as a mobile carboxyl carrier such as pyruvate carboxylase, acetyl CoA carboxylase.

❖In carbohydrate metabolism, biotin functions in both carbon dioxide fixation and decarboxylation, with the energy-producing citric acid cycle dependent on the presence of this vitamin.

❖In protein metabolism, biotin enzymes are important in protein synthesis, amino acid deamination, purine synthesis, and nucleic acid metabolism.



Carbonyl-phosphate
acetyl-CoA carbanion
Malonyl-CoA
ADP
HCO3-
1.
2.
3.
Pi
ACAC
Biotinyl-enzyme
Carboxybiotinyl-enzyme
Biotinyl-enzyme

❖Biotin is important for normal function of the thyroid and adrenal glands, the reproductive tract, and the nervous system.

❖However, the effect of biotin deficiency on the cutaneous system is most dramatic since a severe dermatitis is the major obvious clinical sign of deficiency.

❖Except in infants, there is no evidence of spontaneous biotin deficiency in humans.

❖This is probably due to the ubiquitous nature of the vitamin in diets plus benefits derived from microbial synthesis.

❖Biotin deficiency occurs in individuals consuming a large number of raw eggs daily because of the antagonistic effect of the egg-white protein avidin.

VITAMIN B9, FOLACIN

❖Folacin and folate are generic terms used to describe folic acid and related compounds that exhibit the biological activity of folic acid.

❖A number of researchers in both developed and developing countries have reported a high incidence of folacin deficiency in pregnant women.

❖Because of their rapid growth rate, cancer cells have an exceptionally high folacin requirement.

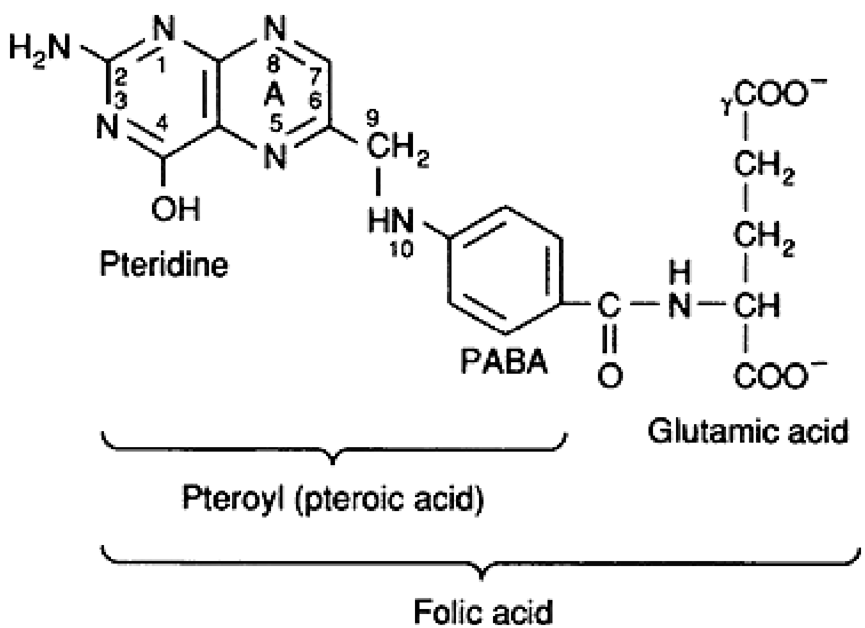
❖Therefore, drugs that inhibit folacin-requiring enzymes are widely used in medicine for cancer chemotherapy.

❖Recent research has shown that adequate serum folacin not only corrects megaloblastic anemia but prevents a number of life threatening diseases, including cardiovascular disease, neural tube defects (e.g., spina bifida and anencephaly), and risk of colorectal and other forms of cancer

❖Folacin is the group name used to distinguish naturally occurring compounds of this class; the pure substance is designated pteroylmonoglutamic acid.

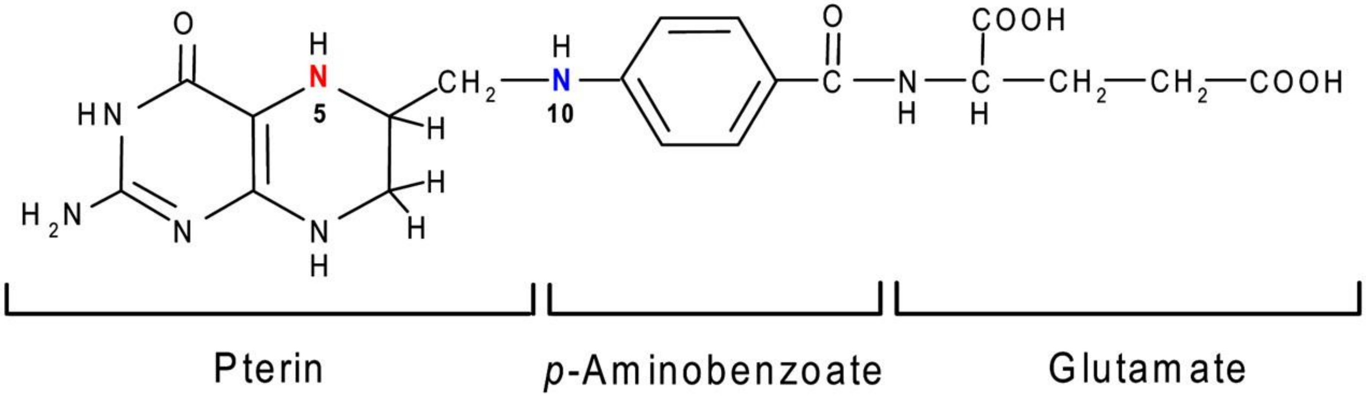
❖The chemical structure of folacin contains three distinct parts. Reading from right to left, this compound consists of glutamic acid, ρ-aminobenzoic acid (PABA), and a pteridine nucleus,

❖The PABA portion of the vitamin structure was once thought to be a vitamin.

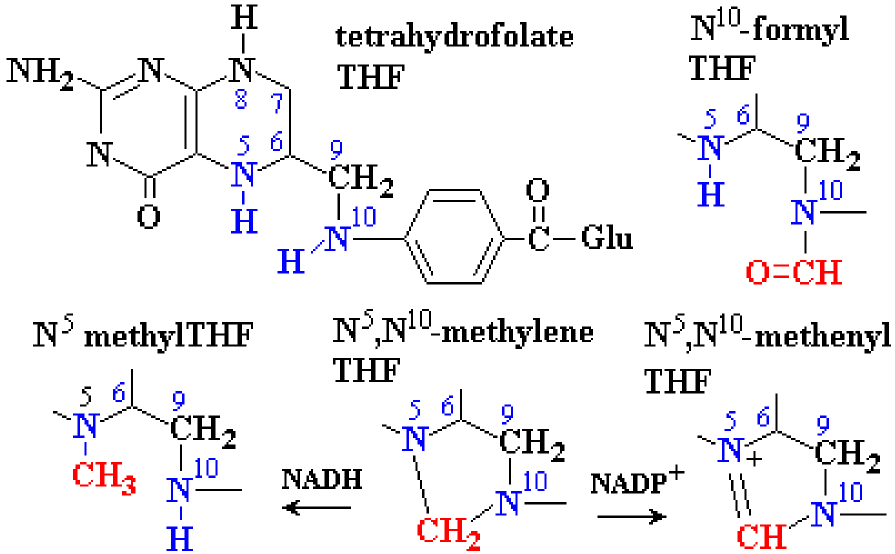


❖Folacin, in the form 5,6,7,8-tetrahydrofolic acid, is indispensable in transfer of single-carbon units in various reactions,—a role analogous to that of pantothenic acid in the transfer of two-carbon units.

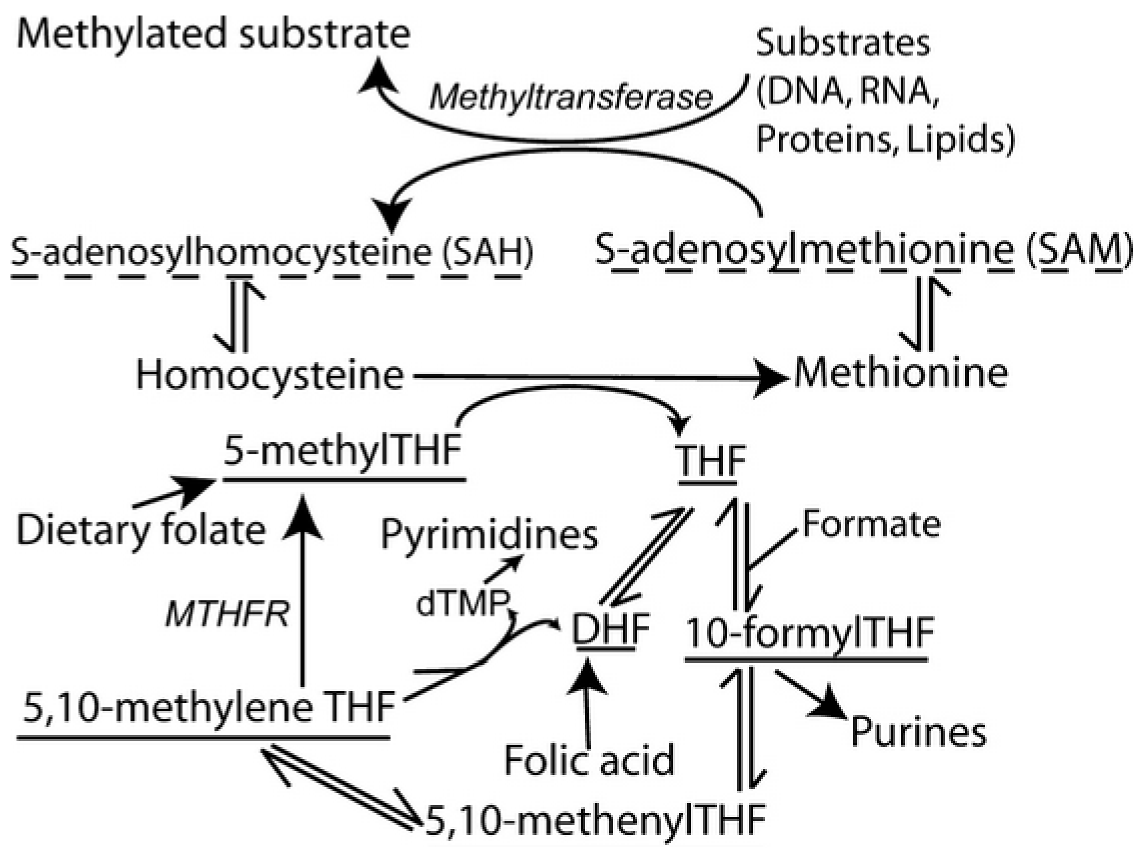
❖The one-carbon units can be formyl, formimino, methylene, or methyl groups.



C_1 unit	Name	Abbreviation
$N^5{-}CH_3$	5-methyl-THF	CH_3-THF
$OHC{-}N^{10}$	10-formyl-THF	10-CHO-THF
$N^5{=}CH{=}N^{10}$	5,10-methenyl-THF	CH=THF
$N^5{-}CH_2{-}N^{10}$	5,10-methylene-THF	CH_2-THF
$N^5{-}CHO$	5-formyl-THF	5-CHO-THF



tetrahydrofolate THF
N10-formyl THF
N5 methylTHF
N5,N10-methylene THF
N5,N10-methenyl THF
NADH
NADP+



Methylated substrate
Substrates (DNA, RNA, Proteins, Lipids)
Methyltransferase
S-adenosylhomocysteine (SAH)
S-adenosylmethionine (SAM)
Homocysteine
Methionine
5-methylTHF
THF
Dietary folate
Pyrimidines
Formate
MTHFR
dTMP
DHF
10-formylTHF
5,10-methylene THF
Purines
Folic acid
5,10-methenylTHF

❖Specific reactions involving single-carbon transfer by folacin compounds are

❖(1) purine and pyrimidine synthesis,

❖(2) interconversion of serine and glycine,

❖(3) glycine-α-carbon as a source of C1 units for many syntheses,

❖(4) histidine degradation, and

❖(5) synthesis of methyl groups for such compounds as methionine, choline, and thymine.

❖For humans, folacin deficiency is probably the most common vitamin deficiency in the world. Infants, adolescents, elderly persons, and pregnant women seem particularly vulnerable.

❖Typical reaction to folacin deficiency in the human is megaloblastic red cell maturation in the bone marrow with resulting macrocytic anemia.

VITAMIN B12, COBALAMIN

❖Vitamin B 12 was the last vitamin to be discovered (1948) and the most potent of the vitamins, with the lowest concentrations required to meet daily requirements.

❖Vitamin B12 is unique in that it is synthesized in nature only by microorganisms; therefore, it is usually not found in plant feedstuffs.

❖Three seemingly unrelated conditions attributed to lack of the vitamin or its precursor were identified: (1) a fatal anemia in humans, (2) a potent growth factor for monogastric species, and (3) a relationship to cobalt, the lack of which resulted in wasting diseases in ruminants.

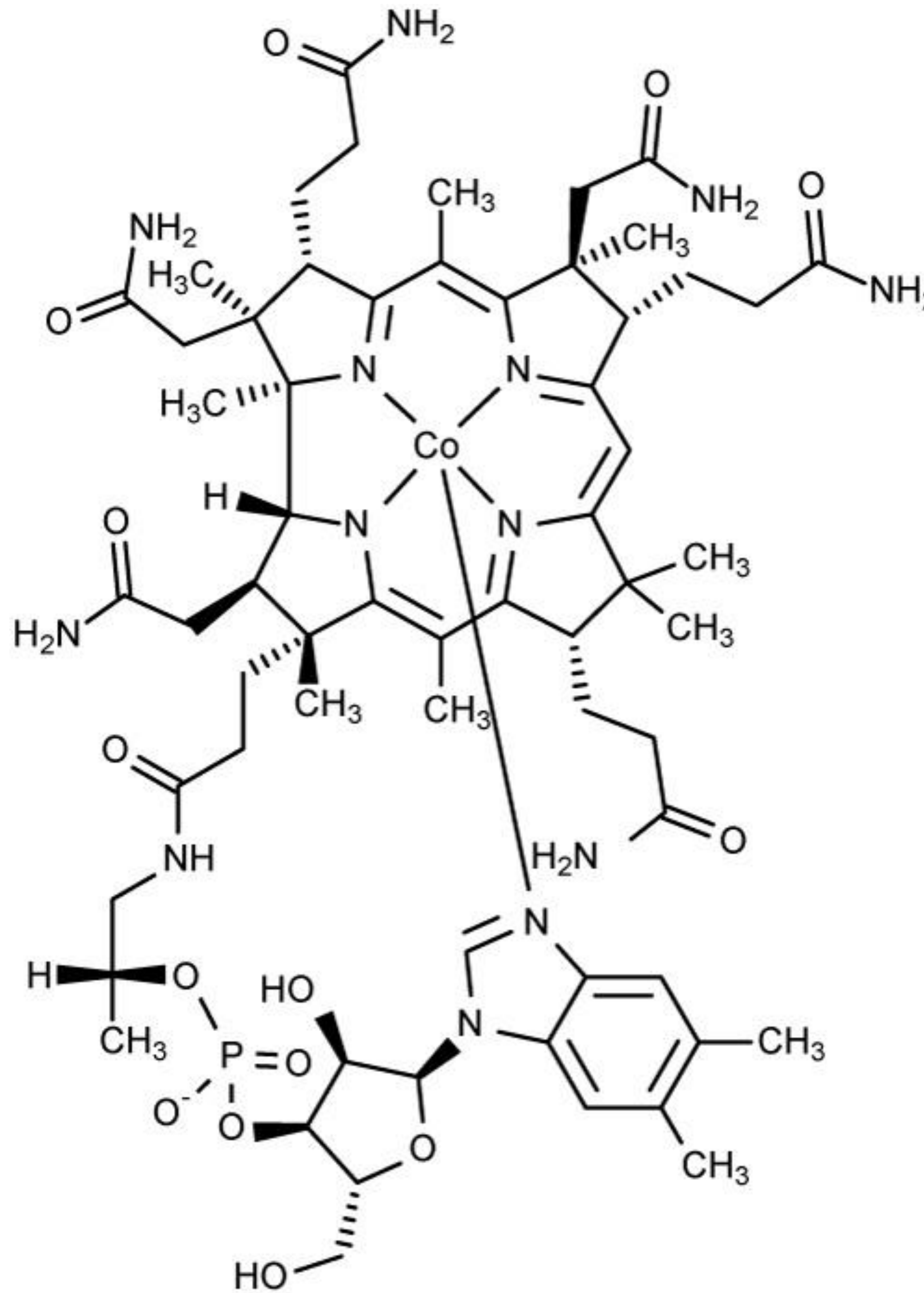
❖Vitamin B 12 is now considered by nutritionists as the generic name for a group of compounds having B12 activity.

❖These compounds have very complex structures.

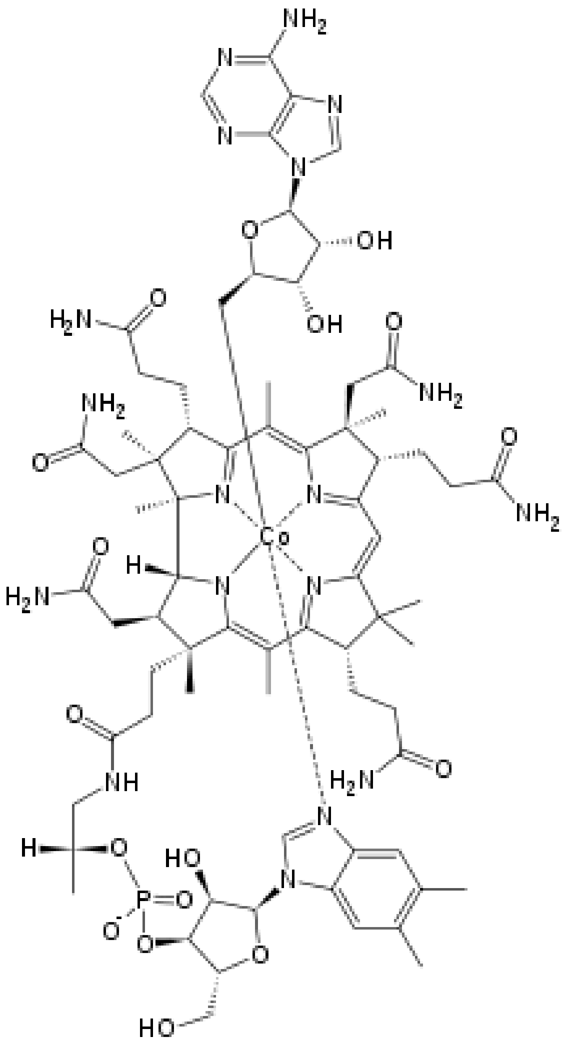
❖Vitamin B12 resembles a porphyrin structure consisting of four pyrrole nuclei coupled directly to each other, with the inner nitrogen atom of each pyrrole coordinated with a single atom of cobalt.

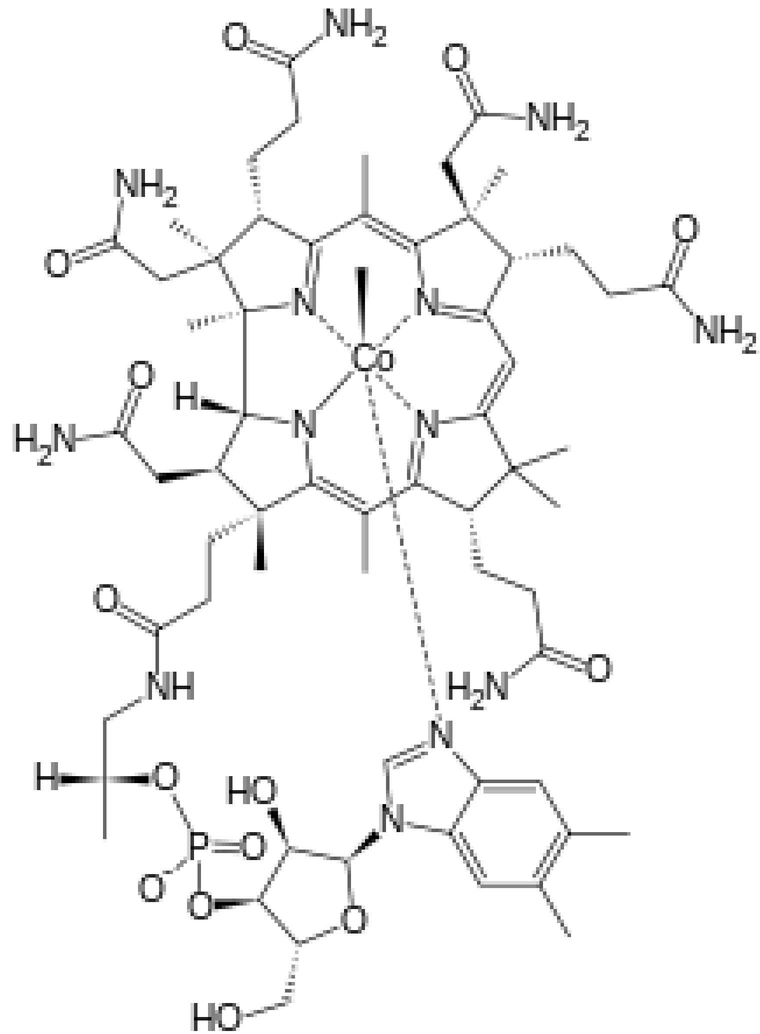
❖The basic tetrapyrrole structure is the corrin nucleus, which positionally is a planar structure coupled below to the nucleotide 5,6-dimethylbenzimidazole and above to cyanide or some other derivative.

❖The large ring formed by the four reduced rings is called “corrin” because it is the core of the vitamin.



❖The two coenzyme forms of cobalamin found in animals are adenosylcobalamin and methylcobalamin.





❖Vitamin B 12 is an essential part of several enzyme systems that carry out a number of very basic metabolic functions.

❖Specific biochemical reactions in which cobalamin coenzymes participate are of two types:

❖(1) those that contain 5´-deoxyadenosine linked covalently to the cobalt atom (adenosylcobalamin) and

❖(2) those that have a methyl group attached to the central cobalt atom (methylcobalamin).

❖There are only two clinically significant reactions in the body that require vitamin B12 as a co-factor.

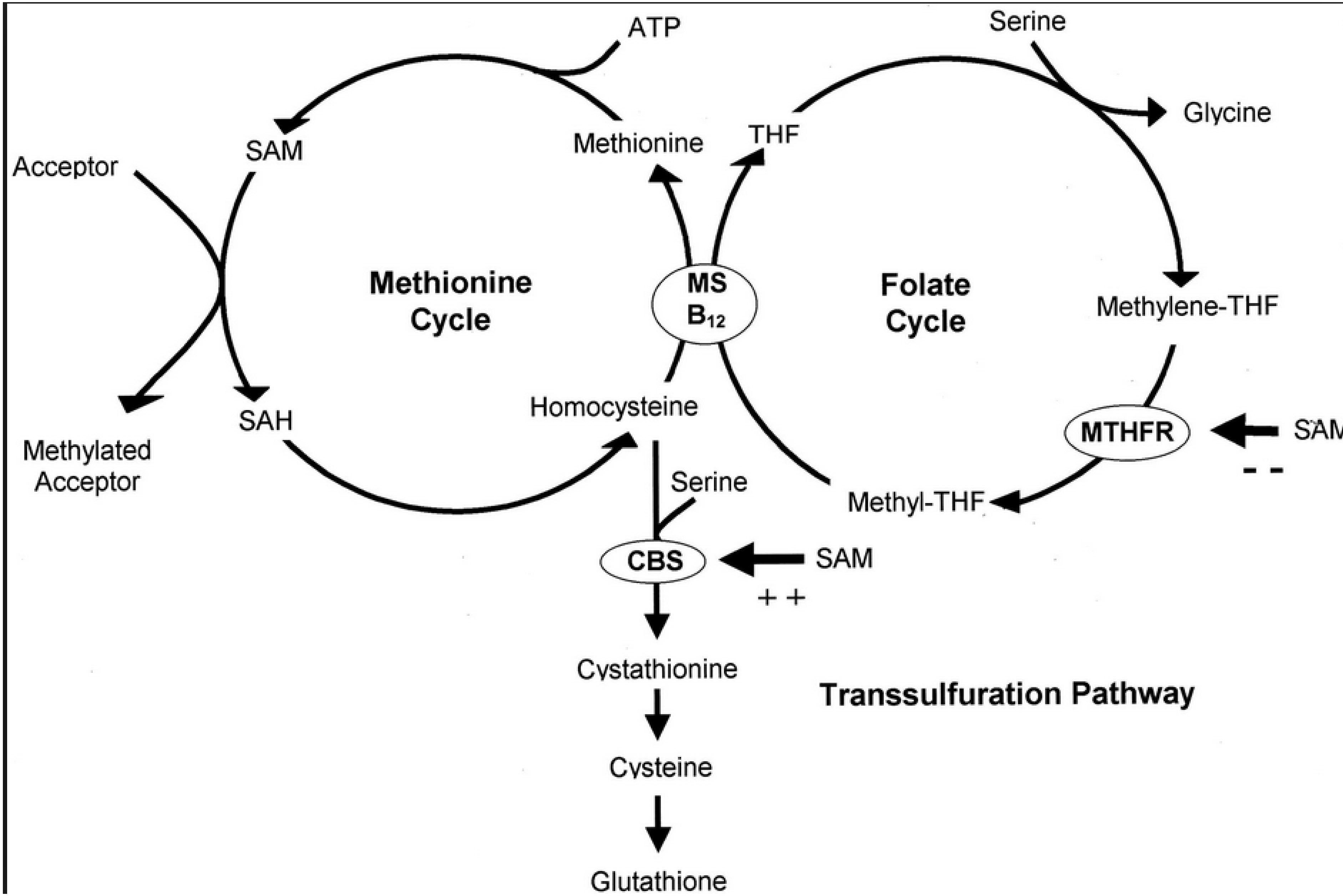
❖During the catabolism of fatty acids with an odd number of carbon atoms and the amino acids valine, isoleucine, methionine, and threonine the resultant propionyl-CoA is converted to succinyl-CoA for oxidation in the TCA cycle.

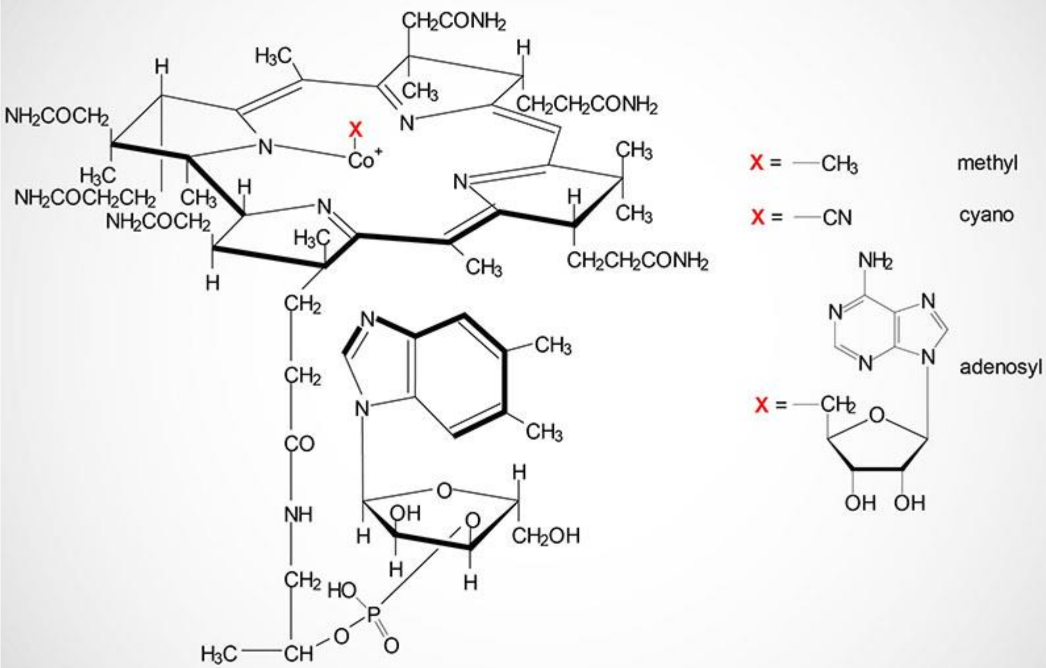
❖One of the enzymes in this pathway, methylmalonyl-CoA mutase, requires vitamin B12 as a cofactor in the conversion of methylmalonyl-CoA to succinyl-CoA.

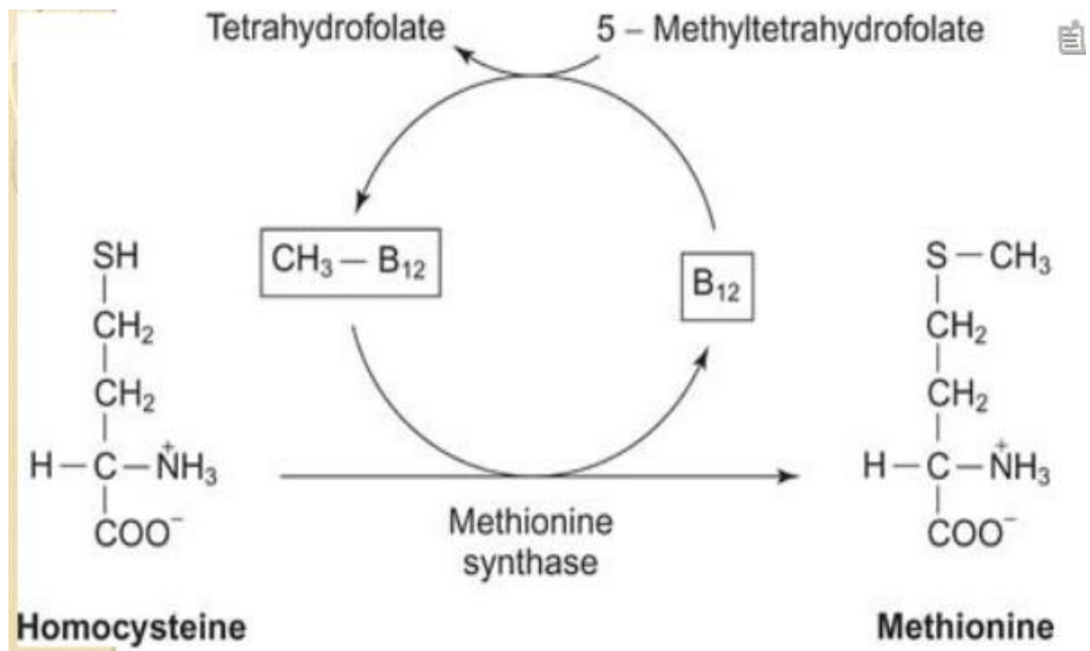
❖The 5'-deoxyadenosine derivative of cobalamin is required for this reaction.

❖The second reaction requiring vitamin B12 catalyzes the conversion of homocysteine to methionine and is catalyzed by methionine synthase (also known as homocysteine methyltransferase).

❖This reaction results in the transfer of the methyl group from N5-methyltetrahydrofolate to hydroxocobalamin generating tetrahydrofolate (THF) and methylcobalamin during the process of the conversion.


ATP
Serine
Glycine
SAM
Methionine
THF
Acceptor
Methionine Cycle
MS
B_{12}
Folate Cycle
Methylene-THF
Methylated Acceptor
SAH
Homocysteine
MTHFR
SAM
- -
Serine
Methyl-THF
CBS
SAM
+ +
Cystathionine
Transsulfuration Pathway
Cysteine
Glutathione


X = —CH3 methyl
X = —CN cyano
X = adenosyl


Tetrahydrofolate
5 – Methyltetrahydrofolate
CH3 — B12
B12
Methionine synthase
Homocysteine
Methionine

❖In humans, pernicious anemia, a fatal megaloblastic anemia with neurological involvement, is the result of vitamin B12 deficiency.

❖In addition to megaloblastic anemia, the most prominent signs and symptoms of vitamin B12 deficiency are weakness, tiredness, lightheadedness, pale and smooth tongue with inflammation, dyspnea, splenomegaly, leukopenia, thrombocytopenia, achlorhydria, paresthesia, neurological changes, loss of appetite, loss of weight, and low serum cobalamin levels.

❖The condition results in stiffness of limbs, progressive paralysis, mental disorders, diarrhea, and finally death.

❖Vitamin B 12 deficiency in humans is influenced by one or more of
❖the following considerations:

❖1. Dietary intake—Inadequate vitamin B12 intake is occasionally seen in geriatric patients and in vegetarians, 2. Failure of absorption or transport and storage.

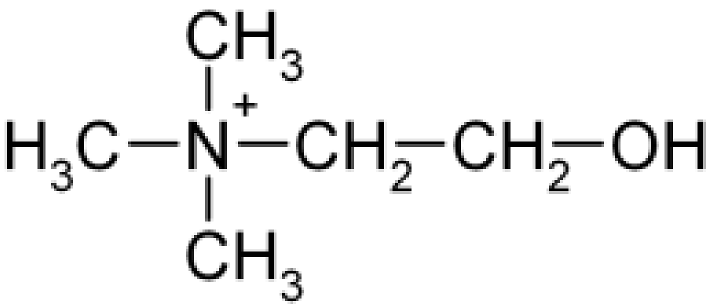
CHOLINE

❖Choline is considered essential to the animal organism and is utilized both as a building unit and as an essential component in regulation of certain metabolic processes.

❖Choline is tentatively classified as one of the B-complex vitamins even though it does not entirely satisfy the strict definition of a vitamin.

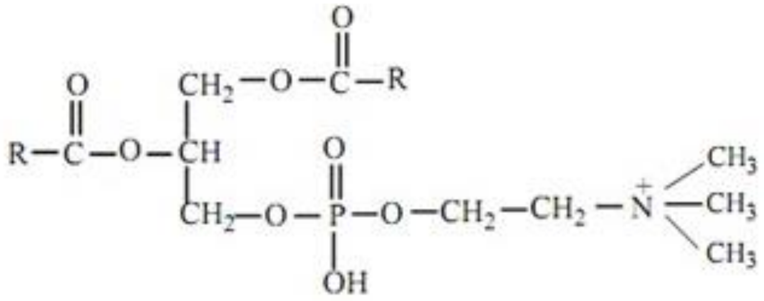
❖Choline, unlike B vitamins, can be synthesized in the liver, is required in the body in greater amounts, and apparently functions as a structural constituent rather than as a coenzyme.

❖Choline is a β-hydroxyethyltrimethylammonium hydroxide and the prominent feature of choline's chemical structure is its triplet of methyl groups, which enables it to serve as a methyl donor.

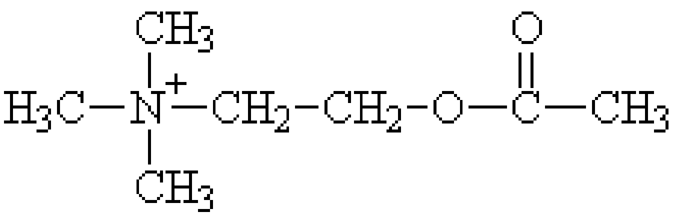


❖Choline is ubiquitously distributed in all plant and animal cells, mostly in the form of the phospholipids phosphatidylcholine.

❖Choline is a precursor for the biosynthesis of the neurotransmitter acetylcholine.



Lecithin



Acetylcholine

❖Choline is a metabolic essential for building and maintaining cell structure.

❖As a phospholipid it is a structural part of lecithin (phosphatidylcholine), certain plasmalogens, and the sphingomyelins.

❖Choline prevents abnormal accumulation of fat (fatty livers) by promoting its transport as lecithin or by increasing the utilization of fatty acids in the liver itself.

❖Choline is essential for the formation of acetylcholine, the agent released at the termination of the parasympathetic nerves.

❖It makes possible the transmission of nerve impulses from presynaptic to postsynaptic fibers of the sympathetic and parasympathetic nervous systems.

❖The demand for choline as a methyl donor is probably the major factor that determines how rapidly a diet deficient in choline will induce pathology.

❖The most common signs of choline deficiency include poor growth, fatty liver, perosis, hemorrhagic tissue (particularly in the kidney and certain joints), and hypertension.

❖Choline is an essential nutrient for humans when excess methionine and folacin are not available in the diet.

❖In humans, high intakes of lecithin or choline produced acute gastrointestinal distress, sweating, salivation, and anorexia.

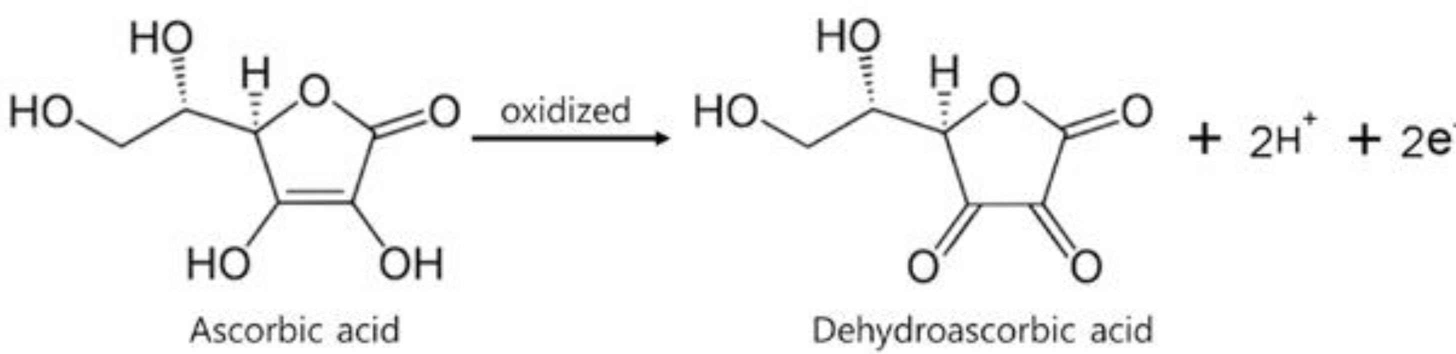
VITAMIN C, ASCORBIC ACID

❖Scurvy, a potentially fatal condition resulting from inadequate vitamin C (ascorbic acid), has been known and feared since ancient times.

❖Vitamin C is synthesized in almost all species, the exceptions being the primates, including humans, guinea pigs, fish, fruit-eating bats, insects, and some birds.

❖Vitamin C primarily occurs in two forms, namely, the reduced ascorbic acid and the oxidized dehydroascorbic acid.

❖The L-isomer of ascorbic acid has activity.



❖Ascorbic acid has been found to be involved in a number of biochemical processes that involve donation of one or two electrons.

❖Function of vitamin C is related to its reversible oxidation and reduction characteristics; however, the exact role of this vitamin in the living system is not clearly known since a coenzyme form has not been reported.

❖ Nevertheless, vitamin C plays important roles in many biochemical reactions, such as mixed-function oxidation involving incorporation of oxygen into the substrate.

❖The most clearly established functional role for vitamin C involves collagen biosynthesis.

❖In addition to the relationship of ascorbic acid to hydroxylase enzymes, Franceschi (1992) suggests that vitamin C is required for differentiation of mesenchyme (embryonic cells capable of developing into connective tissue)-derived connective tissues such as muscle, cartilage, and bone.

- Tissue defense mechanisms against free-radical damage generally include vitamin C, vitamin E, and β-carotene as the major vitamin antioxidant sources.

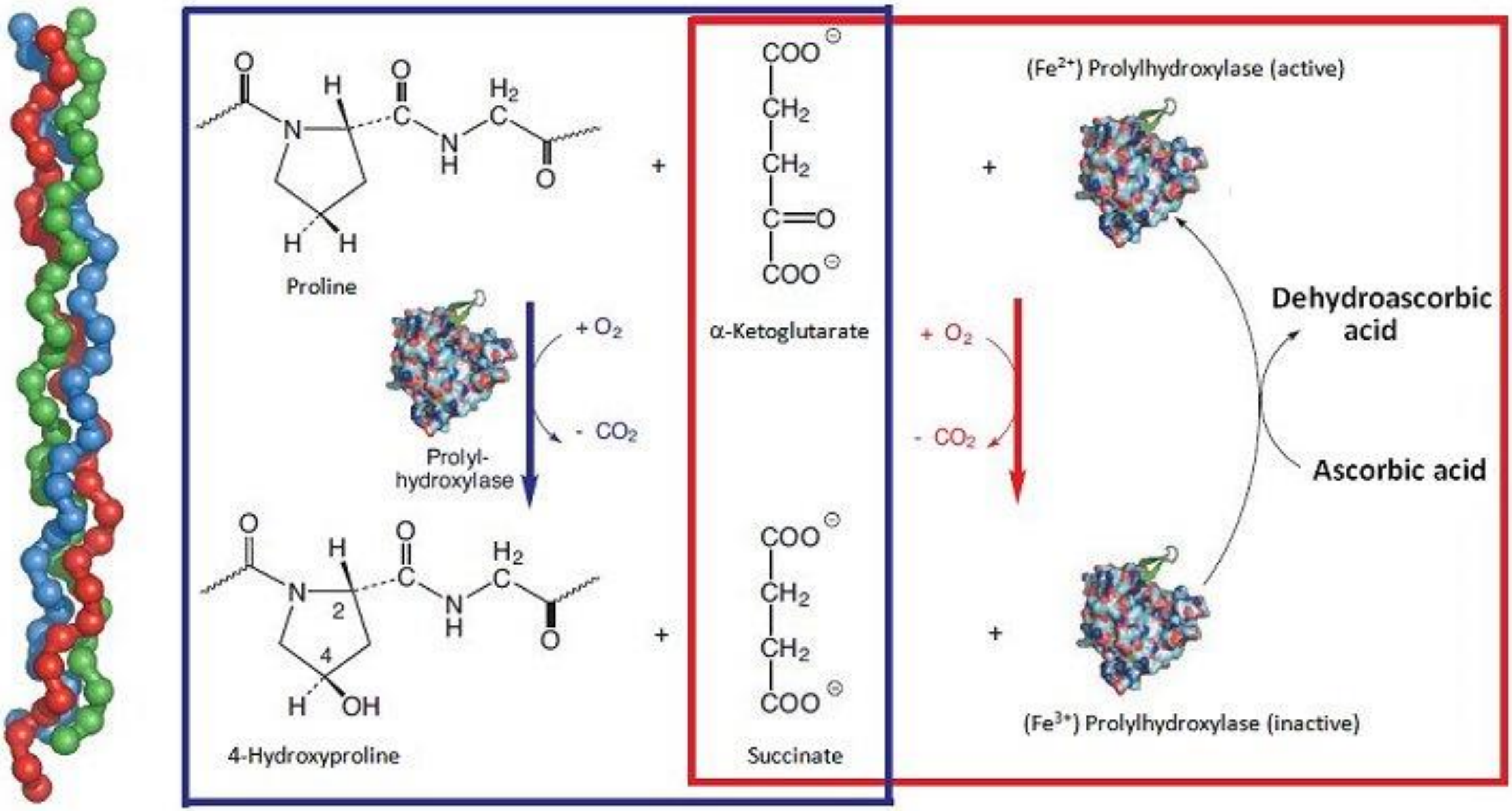
- Vitamin C is the most important antioxidant in extracellular fluids.

- Ascorbic acid is reported to have a stimulating effect on phagocytic activity of leukocytes, on function of the reticuloendothelial system, and on formation of antibodies.

- In humans, gross vitamin C deficiency results in scurvy, a disease characterized by multiple hemorrhages.

- In adults, manifest scurvy is often preceded by lassitude, fatigue, anorexia, muscle pain, and greater susceptibility to infection and stress.

- Scurvy may be fatal, particularly in infants and otherwise debilitated adults.

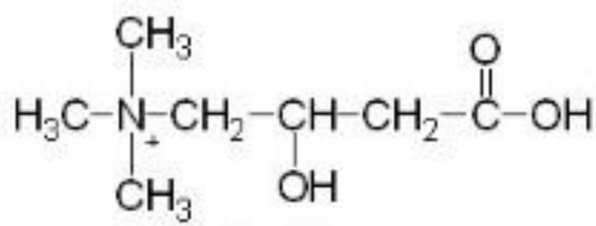

Proline
Prolyl-hydroxylase
+ O2
- CO2
4-Hydroxyproline
α-Ketoglutarate
Succinate
(Fe2+) Prolylhydroxylase (active)
(Fe3+) Prolylhydroxylase (inactive)
Dehydroascorbic acid
Ascorbic acid

CARNITINE

❖Under most conditions for the majority of species, carnitine would not be considered a vitamin as it is adequately synthesized in body tissues.

❖However, the need for supplemental carnitine has been demonstrated in mammals in circumstances in which the biosynthesis is limited by nutritional deprivation of the precursor amino acids lysine and methionine.

❖Carnitine is a quaternary amine, β-hydroxy-γ-trimethylaminobutyrate.



Carnitine

❖Carnitine is an important cofactor for normal cellular metabolism. Optimal utilization of fuel substrates for adenosine triphosphate (ATP) generation by skeletal muscle during exercise is dependent on adequate carnitine stores.

❖Carnitine is required for transport of long-chain fatty acids into the matrix compartment of mitochondria from cytoplasm for subsequent oxidation by the fatty acid oxidase complex for energy production.

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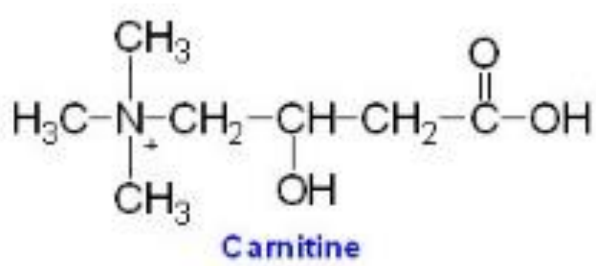

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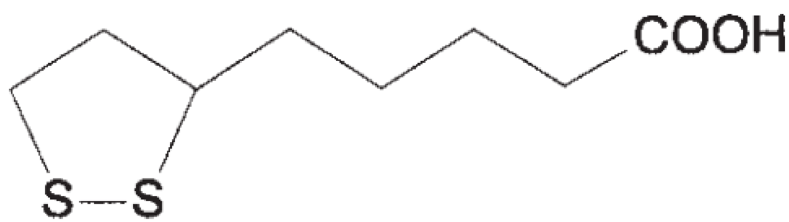
LIPOIC ACID

❖Lipoic acid (thioctic acid) plays an important role in the growth of certain microorganisms.

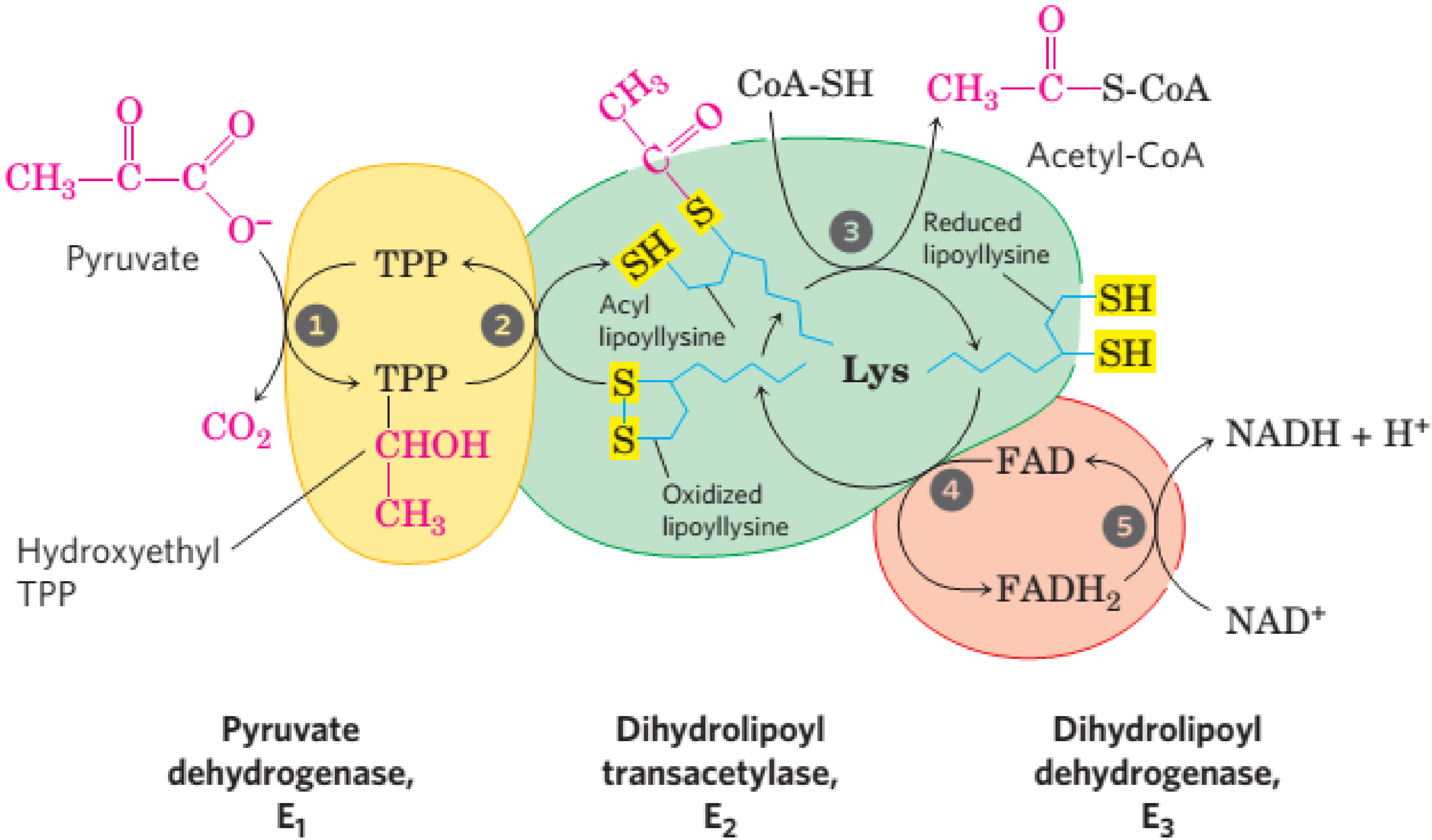
❖Lipoic acid (6-thiocytic acid) is an essential cofactor for the oxidative decarboxylations of α-keto acids where, linked to the ε-amino group of a lysine residue of the enzyme dihydrolipoyl transacetylase, it is one of several prosthetic groups in the multienzyme, lactate dehydrogenase complex.

❖Thus, lipoic acid, occupies a critical position in energy metabolism, regulating the flow of carbon into the tricarboxylic acid cycle.



Lipoic acid

❖The ability to undergo interconversion between disulfide (lipoic acid) and sulfhydryl (dihydrolipoic acid) forms enables this metabolite to function as a metabolic antioxidant.


Pyruvate
TPP
TPP
CHOH
CH3
CO2
Hydroxyethyl TPP
Acyl lipoyllysine
Oxidized lipoyllysine
CoA-SH
Acetyl-CoA
Reduced lipoyllysine
Lys
SH
SH
FAD
FADH2
NADH + H+
NAD+
1
2
3
4
5
Pyruvate dehydrogenase, E1
Dihydrolipoyl transacetylase, E2
Dihydrolipoyl dehydrogenase, E3