Vitamins in Foods

- Animal Foods
  - constant levels
- Plant Foods
  - soil composition, sunlight, moisture, growing conditions, maturity at harvest
- Enrichment: replacing lost nutrients
- Fortification: adding extra nutrients
- Provitamins
  - vitamins in foods in an inactive form

Vitamins

- vitamin requirements are usually expressed as RDA's (recommended dietary allowances)
- guidelines are provided by 2 organizations:
  - the Food and Nutrition Board of the National Academy of Sciences- National Research Council
  - the Food and Drug Administration (FDA)

Vitamin deficiencies

- diminished absorption
  - absorption defect
  - parasites
  - malignancies
- increased requirements
  - rapid growth
  - increased physical activity
  - pregnancy
  - hyperthyroidism
- increased loss
  - drug therapy
  - diuresis
  - lactation

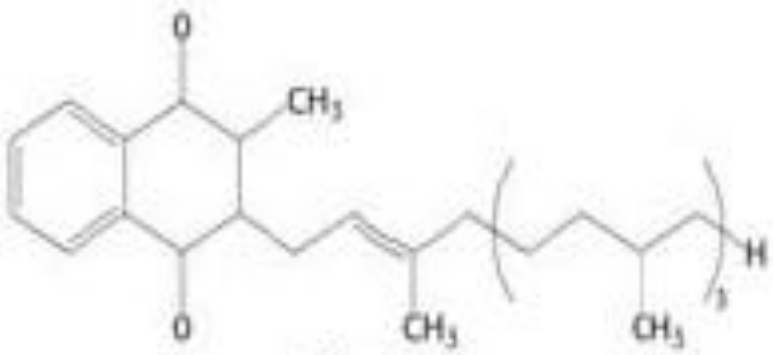
Vitamins, nutritional deficiency diseases

Vitamin	Disease
Ascorbate (C)	Scurvy
Nicotinic acid	Pellagra
Riboflavin (B_2)	Growth retardation
Pantothenate (B_3)	Dermatitis in chickens
Thiamine (B_1)	Beriberi
Pyridoxal (B_6)	Dermatitis in rats
Biotin	Dermatitis in humans
Folate	Anemia
Cobalamin (B_{12})	Pernicious anemia

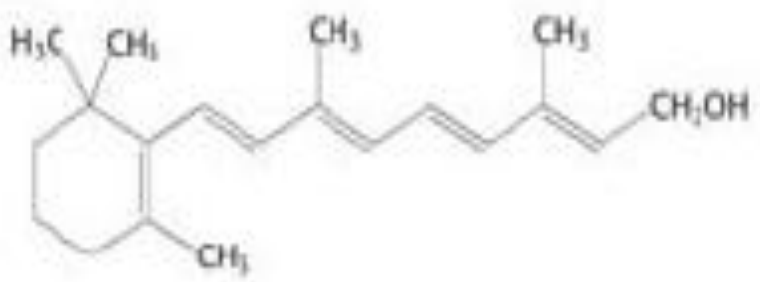
Bogus vitamins

- Vitamin B_4 adenine
- Vitamin B_{10} identical with folic acid
- Vitamin B_{11} . . . .
- Vitamin B_{15} pangamic acid
- Vitamin B_{13} orotic acid
- Vitamin B_{17} laetrile
- Vitamin B_{19} Cheetham's Secret Formula

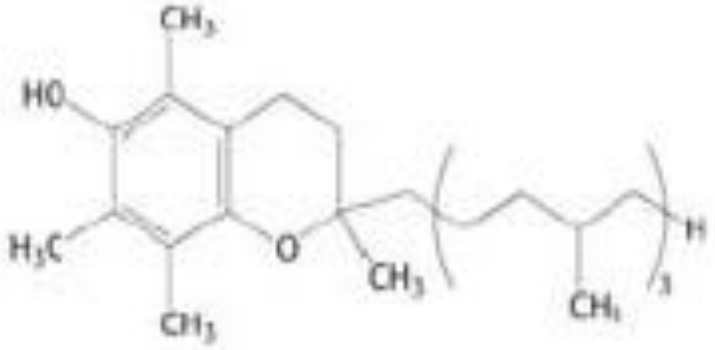
Vitamins - Review



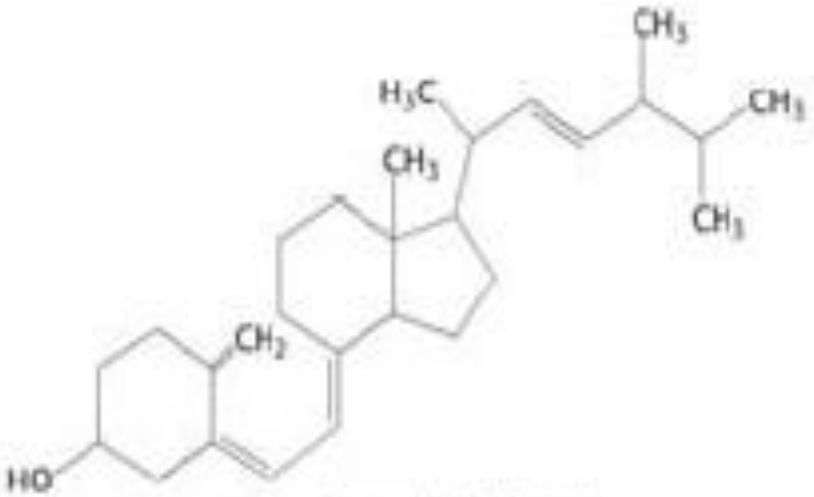
Vitamin K_1



Vitamin A (Retinol)



Vitamin E (α-Tocopherol)



Vitamin D_2 (Calciferol)

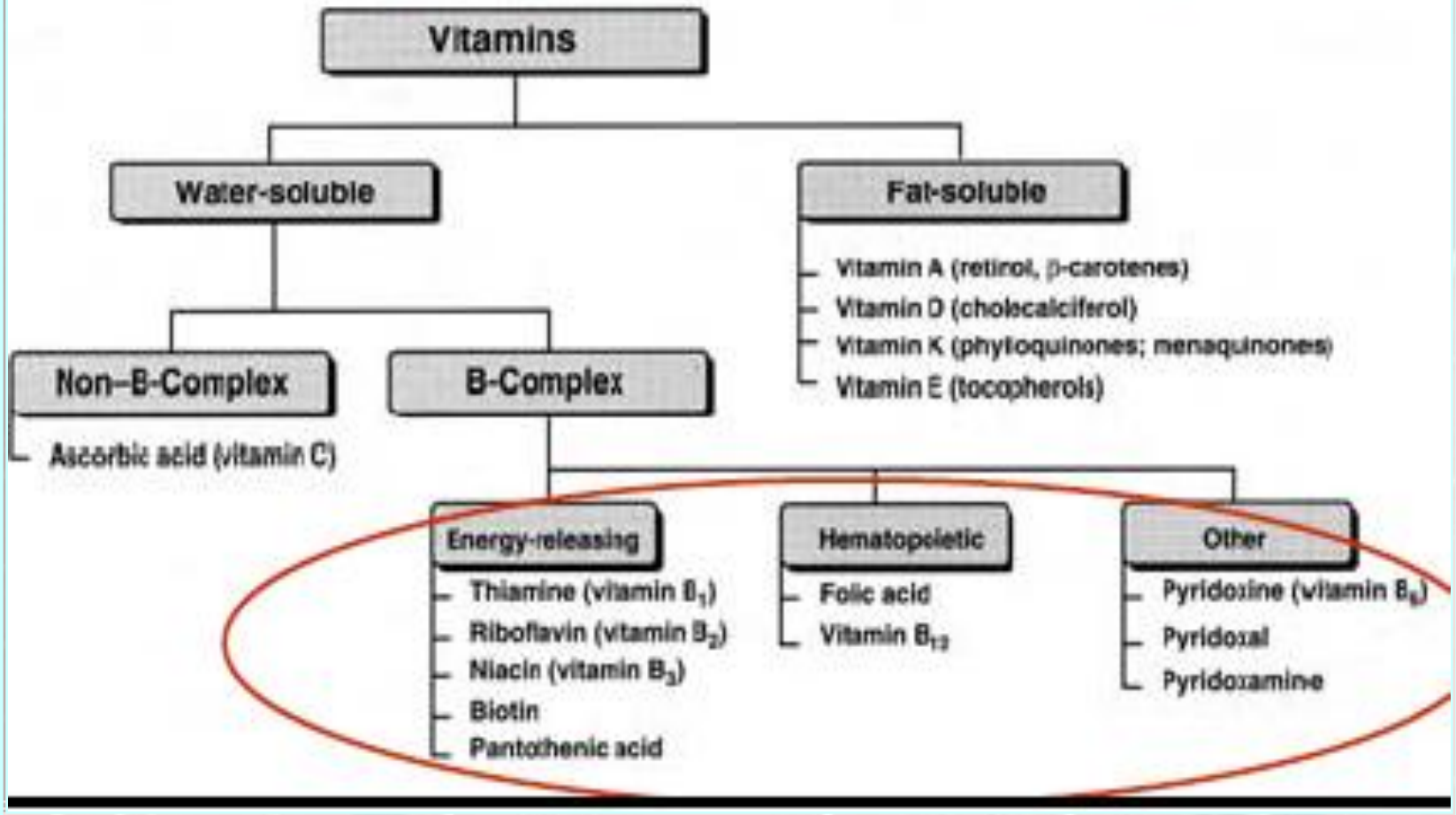
Water Soluble Vitamins

ABLE 8.9 Water-Soluble Vitamins

Vitamin	Coenzyme	Typical reaction type	Consequences of deficiency
Thiamine (B_1)	Thiamine pyrophosphate	Aldehyde transfer	Beriberi (weight loss, heart problems, neurological dysfunction)
Riboflavin (B_2)	Flavin adenine dinucleotide (FAD)	Oxidation–reduction	Cheilosis and angular stomatitus (lesions of the mouth), dermatitis
Pyridoxine (B_6)	Pyridoxal phosphate	Group transfer to or from amino acids	Depression, confusion, convulsions
Nicotinic acid (niacin)	Nicotinamide adenine dinucleotide (NAD^+)	Oxidation–reduction	Pellagra (dermatitis, depression, diarrhea)
Pantothenic acid	Coenzyme A	Acyl-group transfer	Hypertension
Biotin	Biotin–lysine complexes (biocytin)	ATP-dependent carboxylation and carboxyl-group transfer	Rash about the eyebrows, muscle pain, fatigue (rare)
Folic acid	Tetrahydrofolate	Transfer of one-carbon components; thymine synthesis	Anemia, neural-tube defects in development
B_{12}	5′-Deoxyadenosyl cobalamin	Transfer of methyl groups; intramolecular rearrangements	Anemia, pernicious anemia, methylmalonic acidosis
C (ascorbic acid)		Antioxidant	Scurvy (swollen and bleeding gums, subdermal hemorrhages)

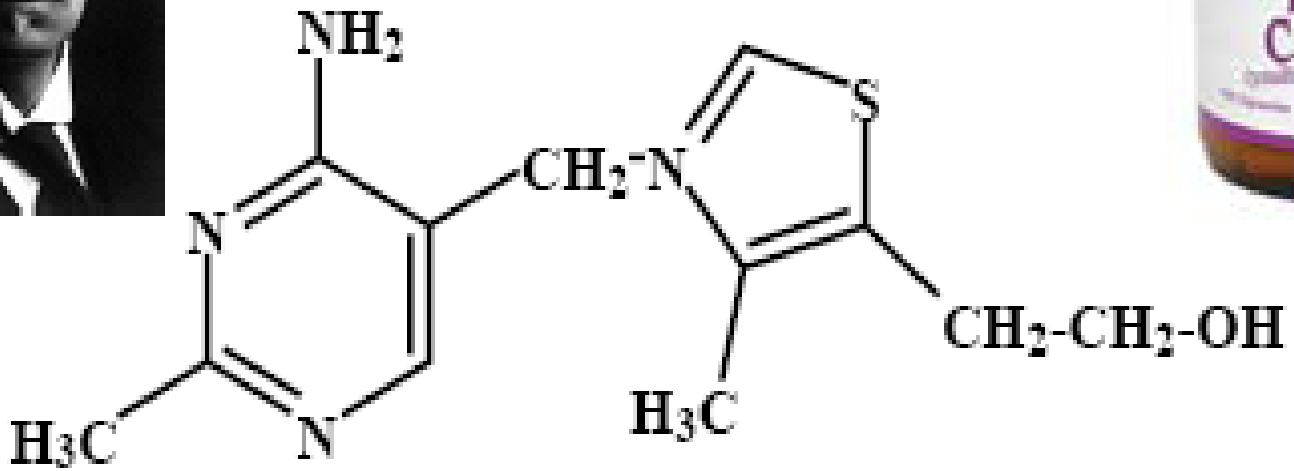
The B vitamins serve as enzyme cofactors

(only catalytic quantities are necessary)



1- THIAMINE (B1)

Thiamine

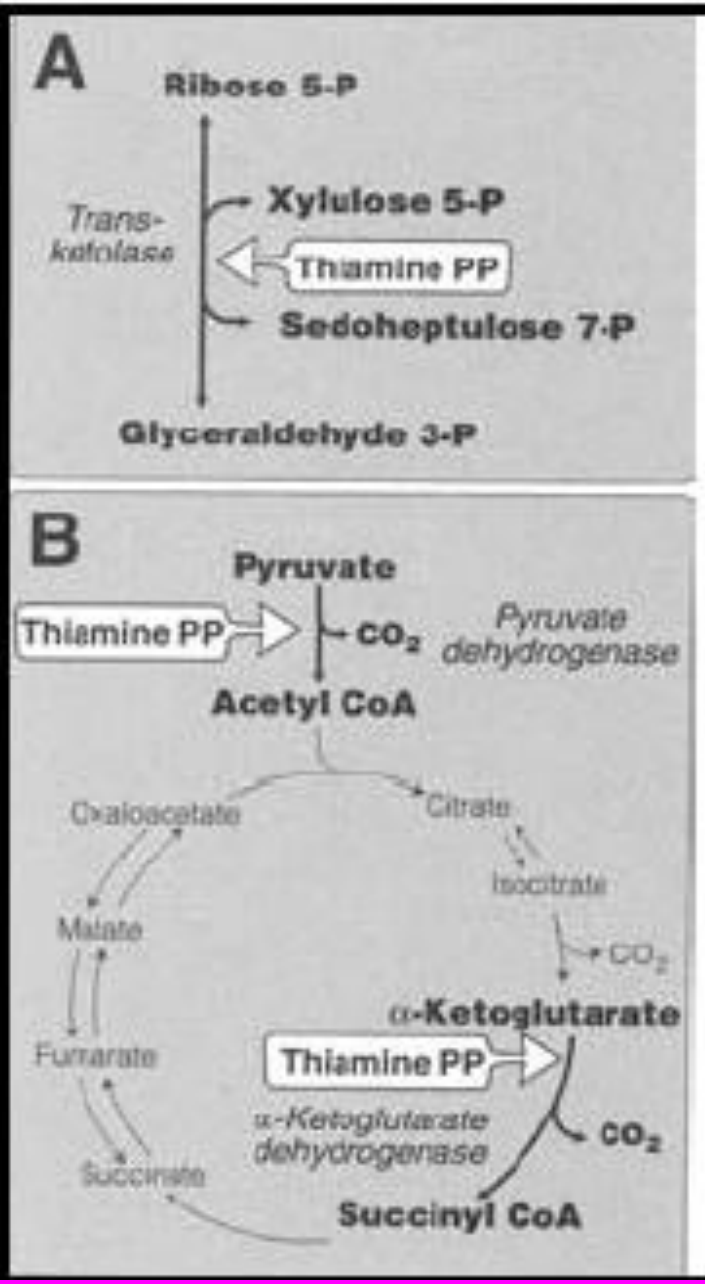


THIAMINE

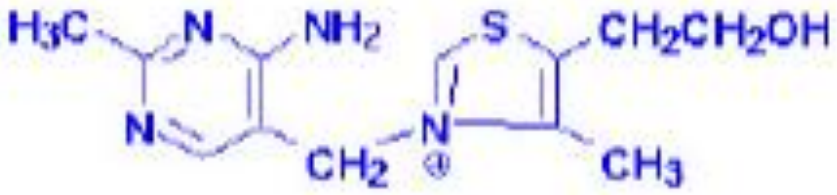
Vitamin B_1; antiberi-beri vitamin; antineuritic factor was the first water soluble vitamin discovered (Eijkman)

Thiamine

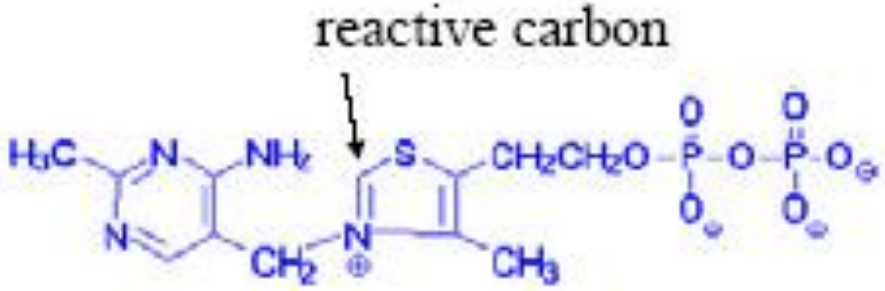
- active form is thiamine pyrophosphate (formed by the action of thiamine diphosphotransferase)
- involved in the oxidative decarboxylation of pyruvic acid and α-ketoglutaric acid
- involved in the transketolase reactions of the triose phosphate pathway
- also required for nerve function (unrelated to coenzyme activity)



Thiamine - Vitamin B_1

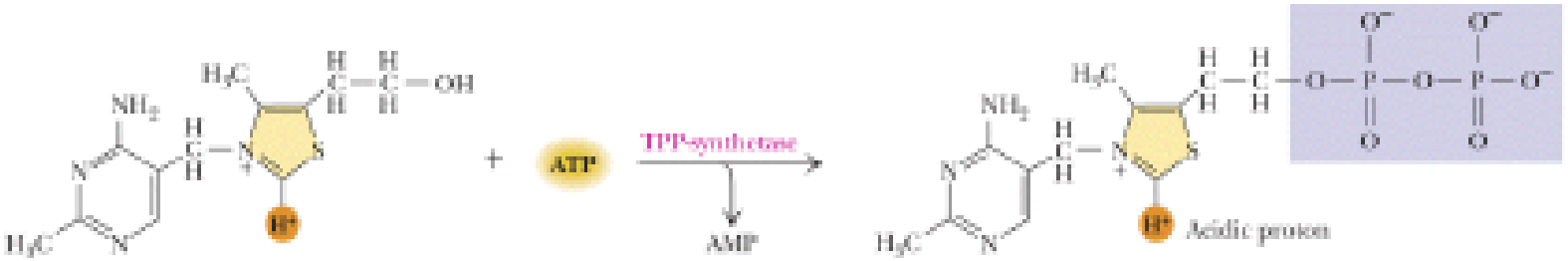


Thiamine is converted into the active form thiamine pyrophosphate or TPP.



TPP is critical in three central reactions (alcohol transfers) in energy release from carbohydrates.

Thiamine (Vitamin B1)



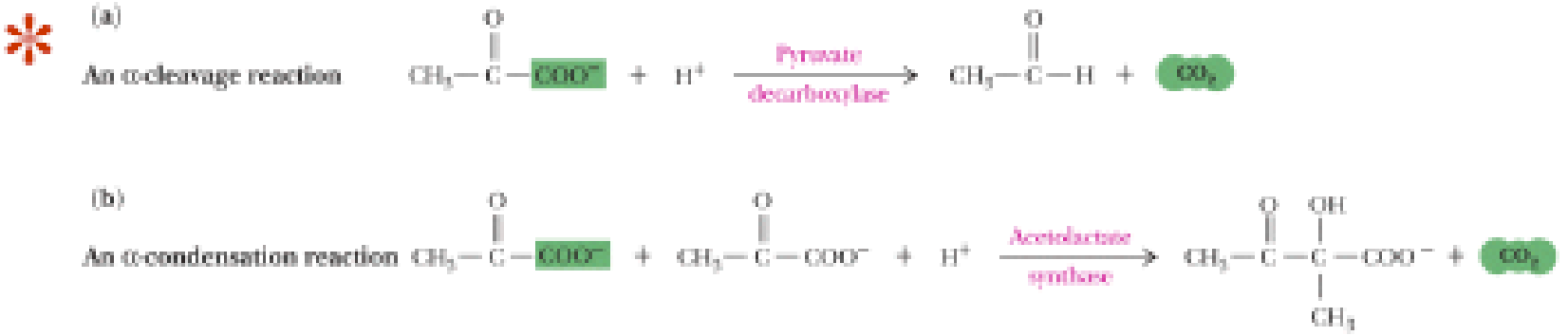
Thiamine (vitamin B_1)

Thiamine pyrophosphate (TPP)

Thiamine pyrophosphate (TPP) is active form

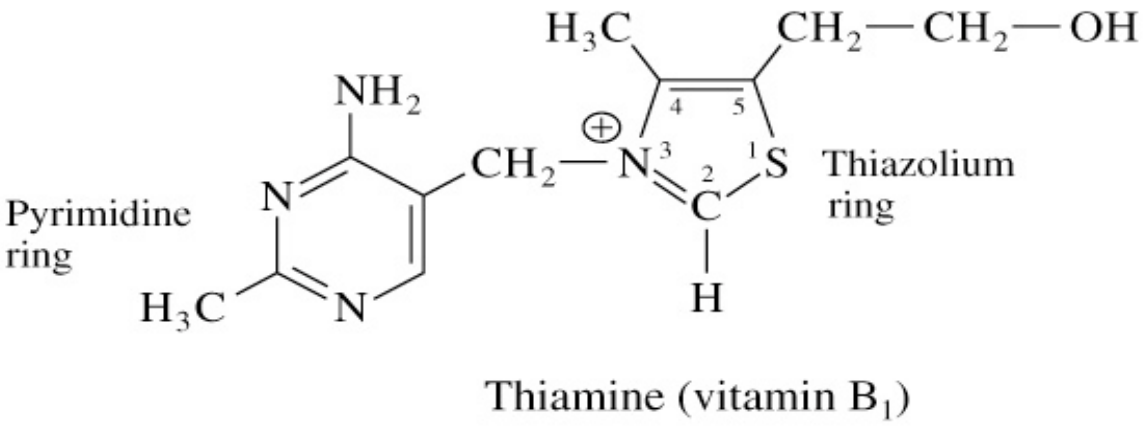
Cofactor in decarboxylations when COO^- is next to carbonyl

Garrett/Grisham, Biochemistry with a Human Focus
Figure 14.15



* Important reaction

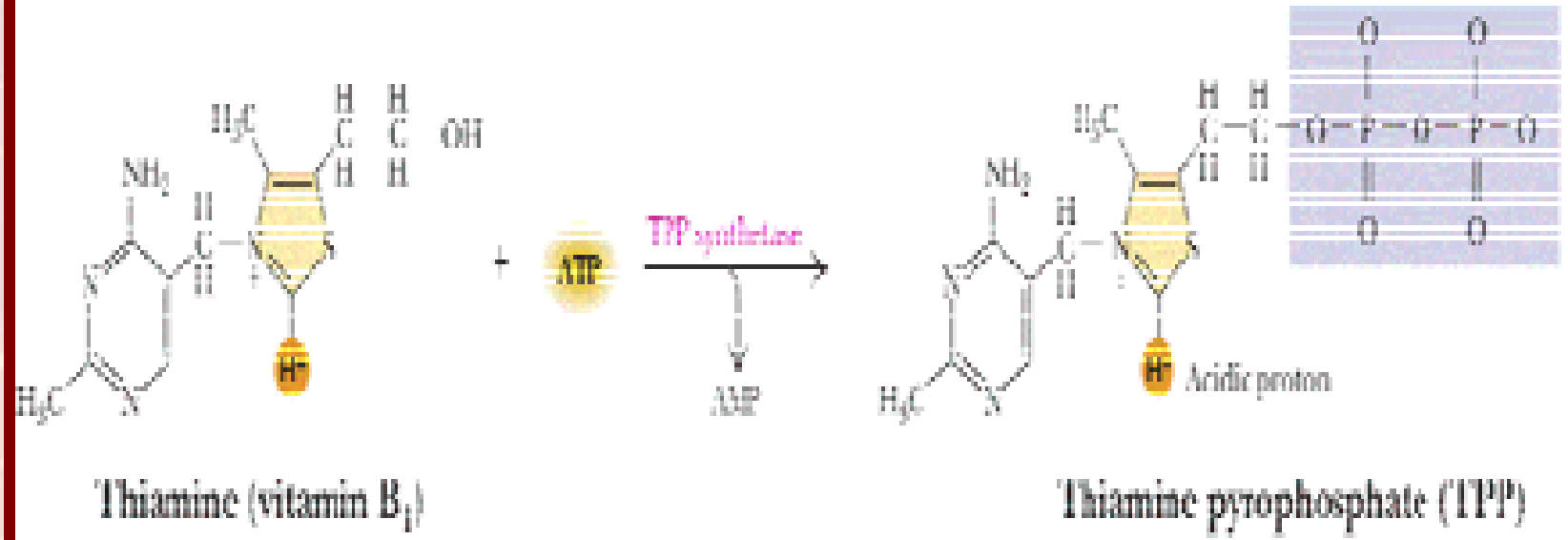
Thiamine (Vitamin B_1) and TPP



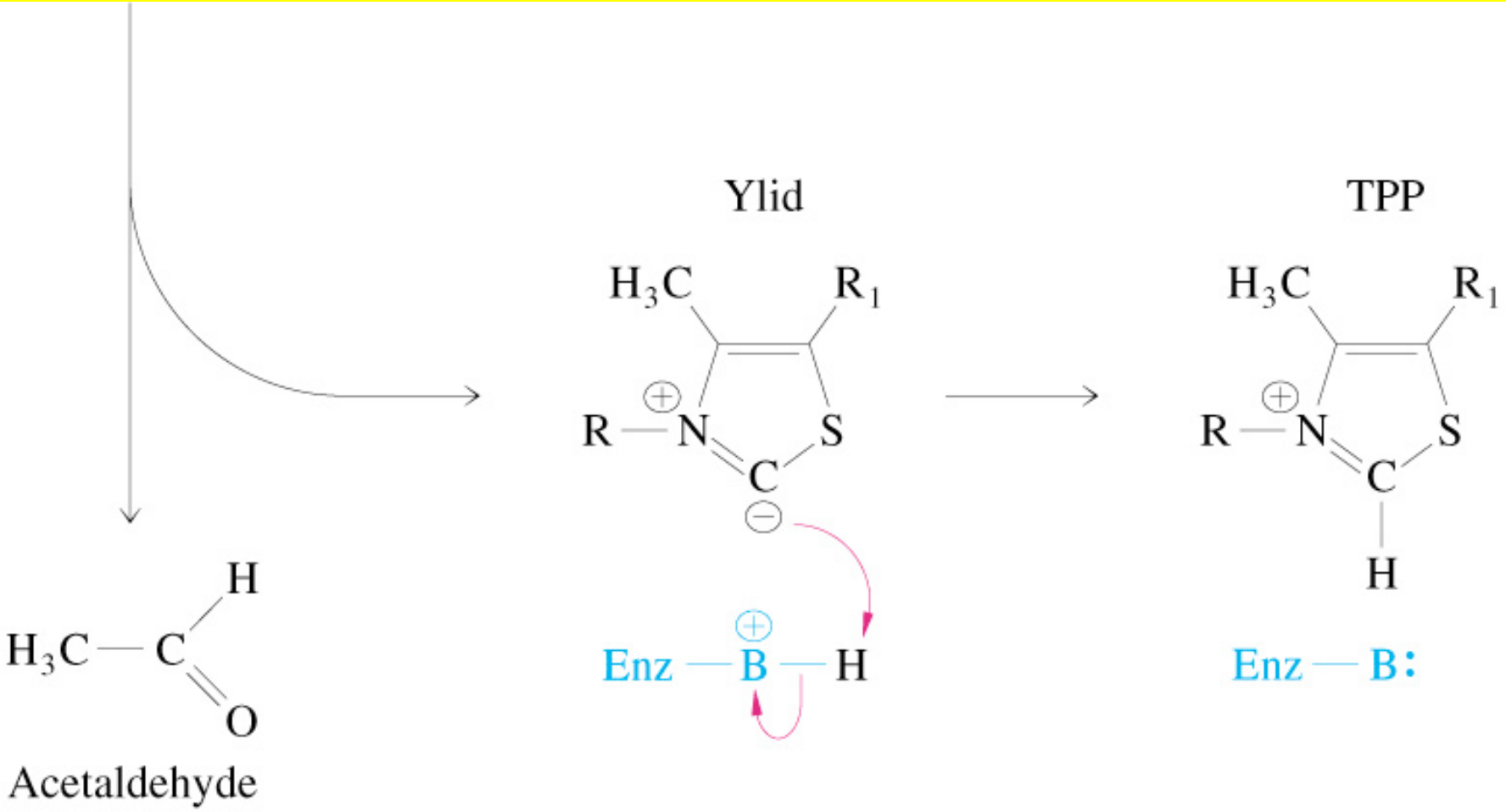
Thiamine Pyrophosphate (TPP)

- TPP is a derivative of thiamine (Vit B_1)
- Reactive center is the thiazolium ring (with a very acidic hydrogen atom at C-2 position)
- TPP participates in reactions of:
  (1) Decarboxylation
  (2) Oxidative decarboxylation
  (3) Transketolase enzyme reactions

Conversion of thiamine to TPP



Mechanism of pyruvate dehydrogenase



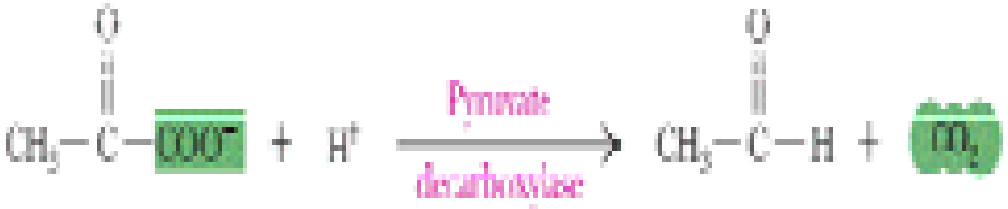
Reactions in which thiamine pyrophosphate is a cofactor

- Pyruvate decarboxylase
  - Alcohol fermentation – pyruvate to acetaldehyde
- Pyruvate dehydrogenase
  - Synthesis of acetyl-CoA
- Alpha-ketoglutarate dehydrogenase
  - Citric acid cycle
- Transketolase reaction
  - Carbon-fixation reactions of photosynthesis
- Acetolactase synthetase
  - Valine, leucine biosynthesis

Typical reactions catalyzed by TPP

(a)

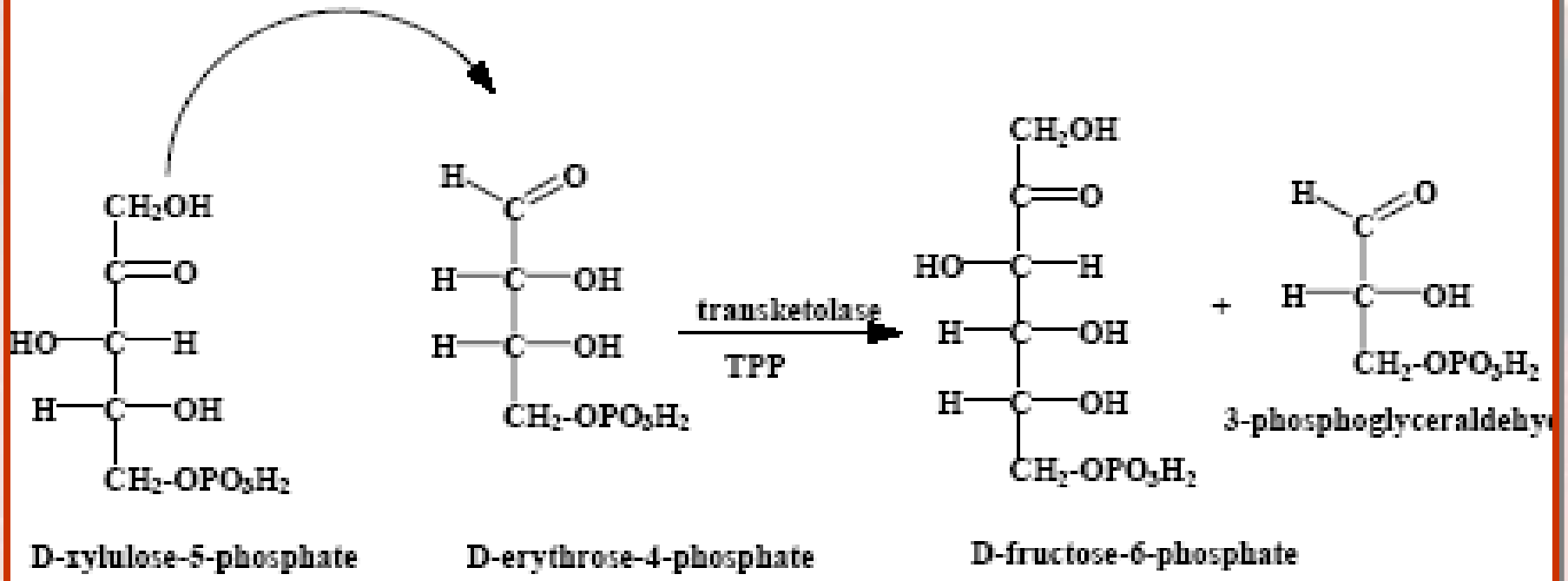
An α-cleavage reaction



(b)

An α-condensation reaction

Transketolase reaction



These reactions provide a link between the pentose phosphate pathway and glycolysis

Activity of erythrocyte transketolase is commonly used as an index of thiamine deficiency

Requirement for thiamine

- Based on energy needs
  - 0.3 – 0.6 mg/1000 calories
  - Increased requirements:
    - Pregnancy and lactation
    - Eating large amounts of raw sea food (clams) – contain thiaminase
    - Stress situations (high level of exercise, fever, hyperthyroidism)
    - Drinking large quantities of tea (contains antagonist)

Thiamine deficiency

- Thiamine intake needs to be proportional to carbohydrate intake.
- Diagnosis: increase in erythrocyte transketolase activity upon thiamine-PP addition
- BeriBeri: severe deficiency usually caused by high carbs/low thiamine diet.
- Alcoholics often have a thiamine deficiency: **Wernicke's Encephalopathy.**
- Symptoms: constipation, appetite suppression, nausea as well as mental depression, peripheral neuropathy and fatigue.

Thiamine deficiency

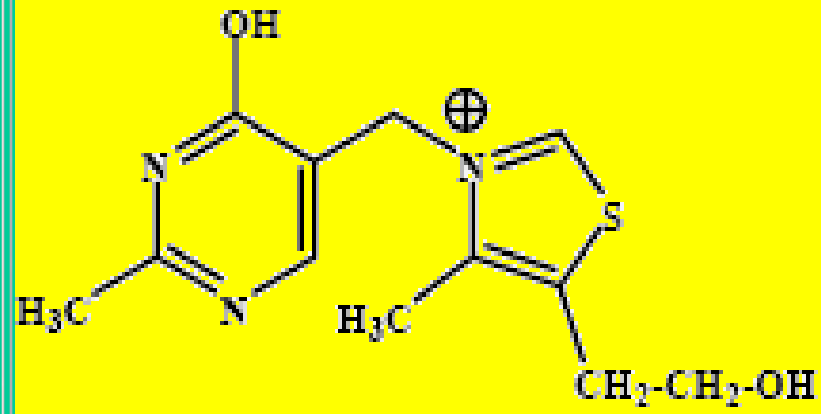
- earliest symptoms of thiamine deficiency include:
  - constipation
  - appetite suppression
  - nausea
  - mental depression
  - peripheral neuropathy
  - fatigue

Thiamine deficiency (severe)

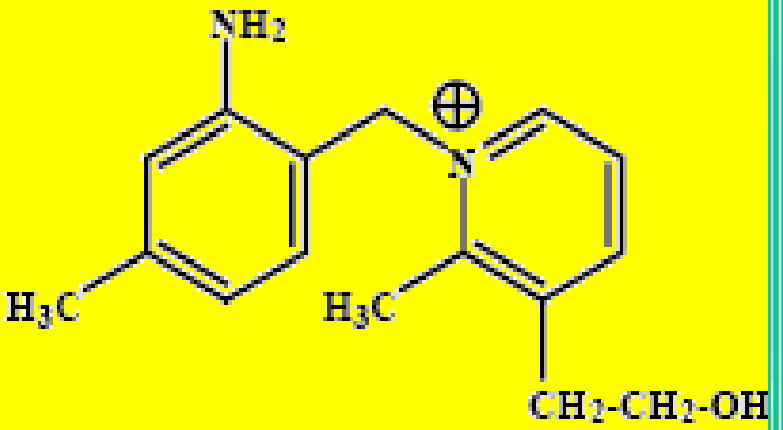
- beri-beri (once associated with white polished rice diets and with highly milled wheat diets)
- 2 clinical types
  - dry beri beri or neuritic beriberi
    - associated with polyneuropathy (depressed peripheral nerve function, sensory disturbance, loss of reflexes and motor control and muscle wasting
  - wet beri beri or cardiovacular beriberi
    - edema, congestive heart failure

So, What is the Treatment ??

Anti-Thiamine Agents



OXYTHIAMINE



NEOPYRITHIAMINE

These 2 compounds are potent antithiamine agents which may be used to induce symptoms of vitamin B_1 deficiency in selected animals. Oxythiamine competitively inhibits thiamine pyrophosphate and becomes active after phosphorylation; neopyrithiamine prevents the conversion of thiamine to thiamine pyrophosphate

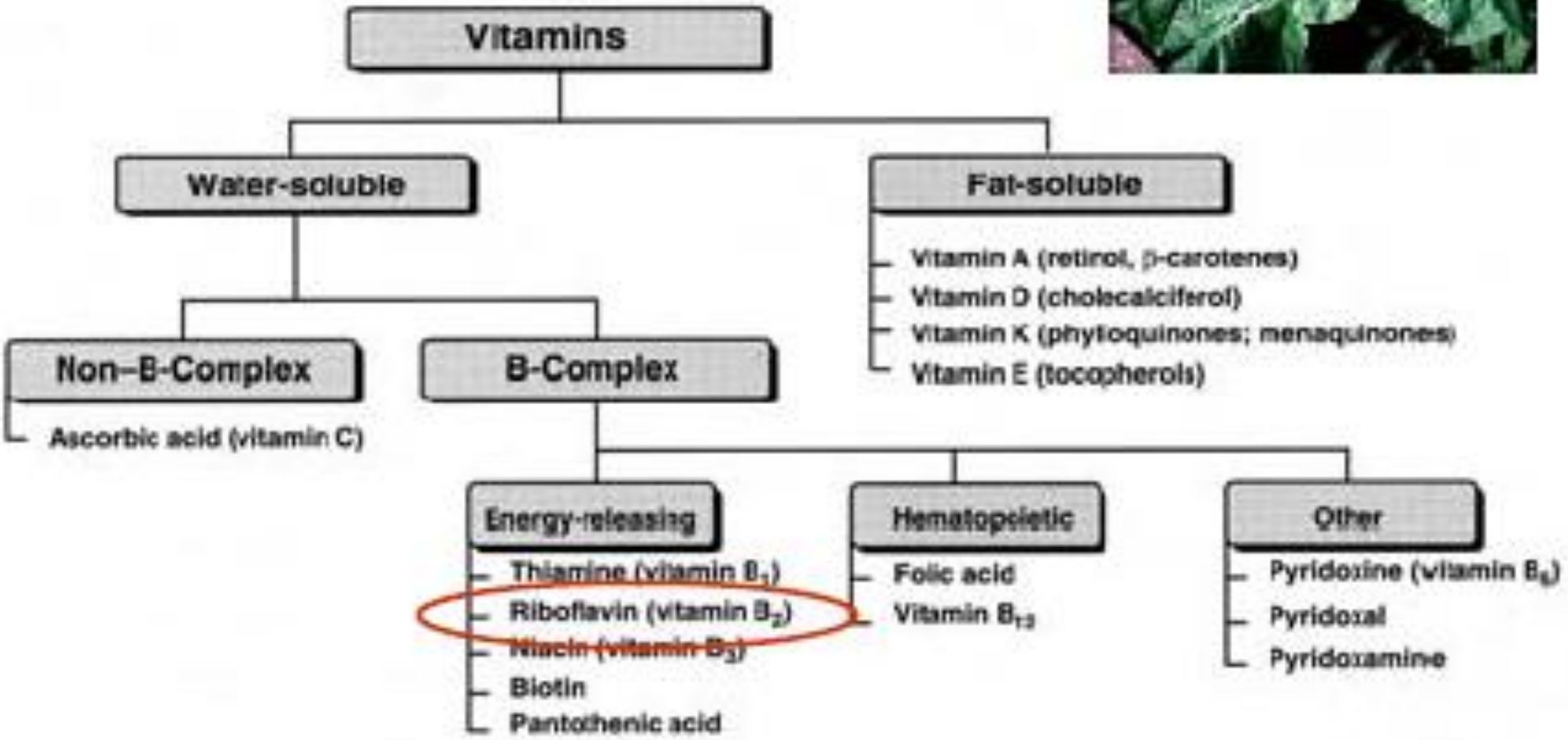
Other clinical applications

- Alcoholic neuritis (peripheral neuropathy)
  - Also a complication of chronic/heavy use of alcohol
  - Usually follows DT's (delirium tremens)
  - Coarse tremors, foot drop
- Wernicke's encephalopathy
  - Disorientation
  - Ocular palsies
  - Complete or partial ophthalmoplegia
- Korsakoff's syndrome or psychosis
  - Sharp burning pain in the feet
  - Deep muscle tenderness with numbness
  - Memory loss
  - Delusions
  - Degeneration of basal ganglia due to chronic/heavy use of alcohol
  - Rigidity of extremities
- Combined Wernicke-Korsakoff syndrome
- Pregnancy neuritis
- Certain gastrointestinal disorders
  - Nausea and vomiting

2-Riboflavin (B2)

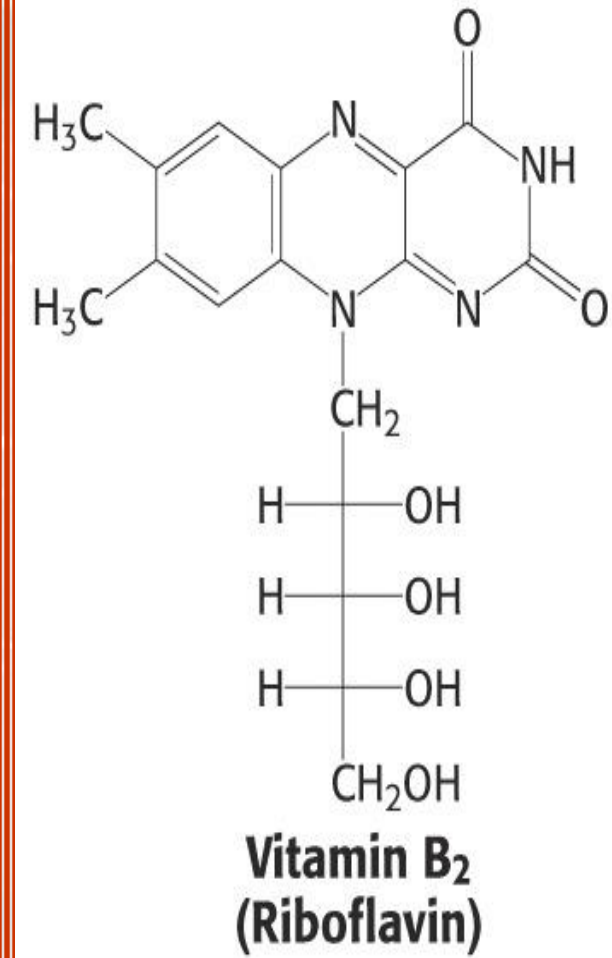
Vitamin B_2

Nutritional sources include:
Milk, eggs, liver, green leafy vegetables



Riboflavin

- Vitamin B2
- Water-soluble
- Required for metabolism of amino acids, fatty acids, and carbohydrates.
- Activates Vitamin B6 (pyridoxine)
- Found in meats, nuts, cheese, milk, leafy vegetables, fish, legumes, grains
- Not toxic in high doses (but turns urine dark yellow)
- Deficiency (not common) seen in eye and skin disorders, mouth inflammation.

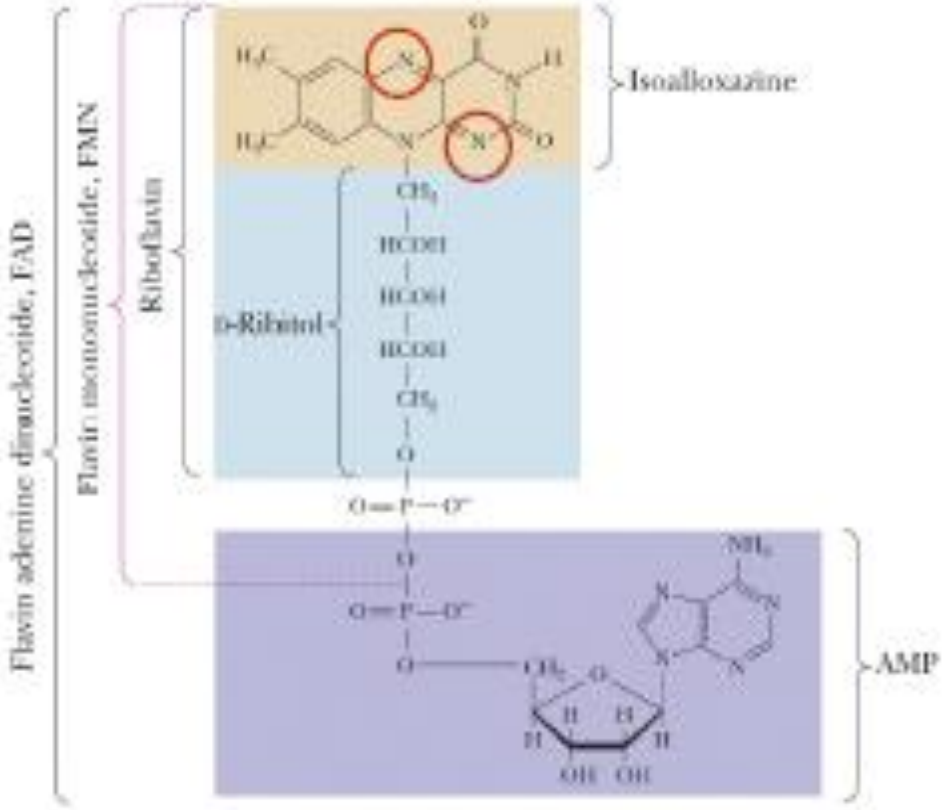


Vitamin B_2
(Riboflavin)

Riboflavin (Vitamin B2)

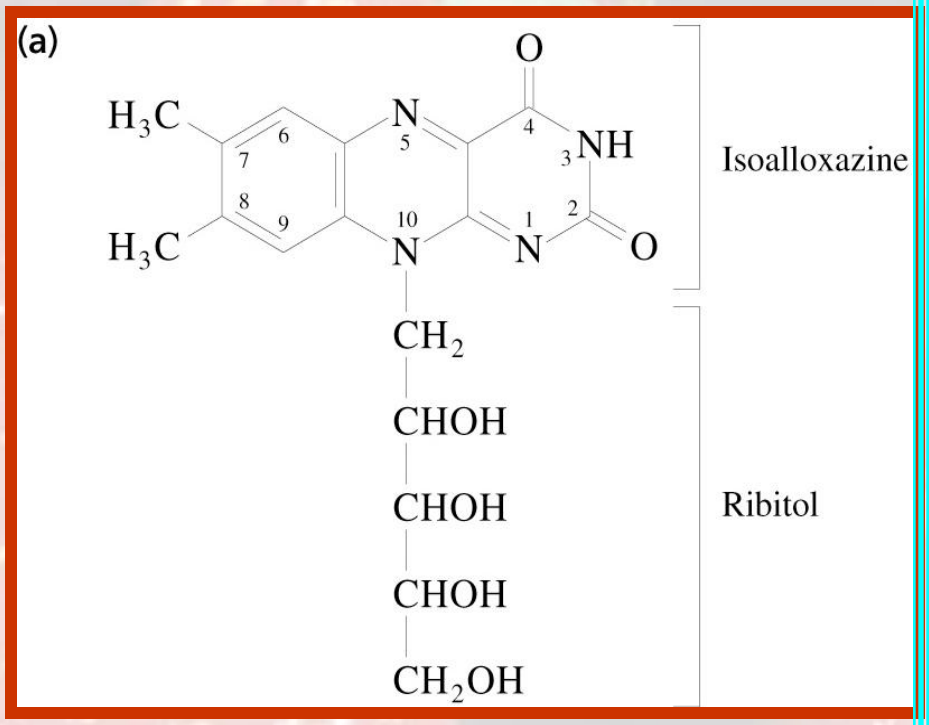
Garrett/Grisham, Biochemistry with a Human Focus
Figure 14.17

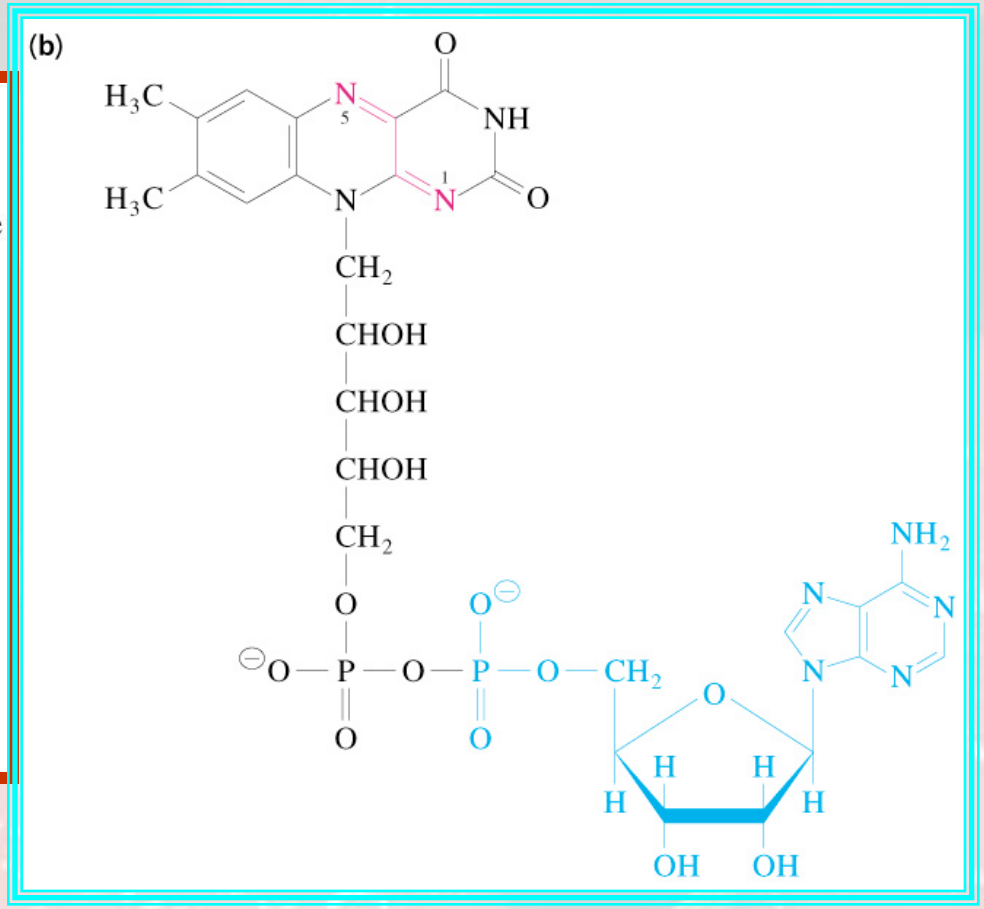
Also involved in redox reactions
And electron transport

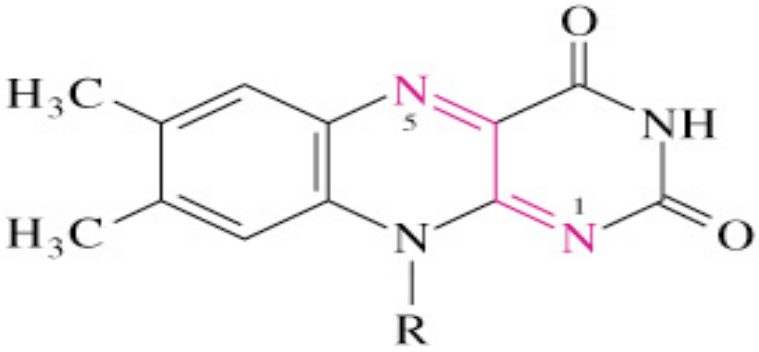


Riboflavin and its coenzymes

(a) Riboflavin, (b) FMN (black), FAD (black/blue)

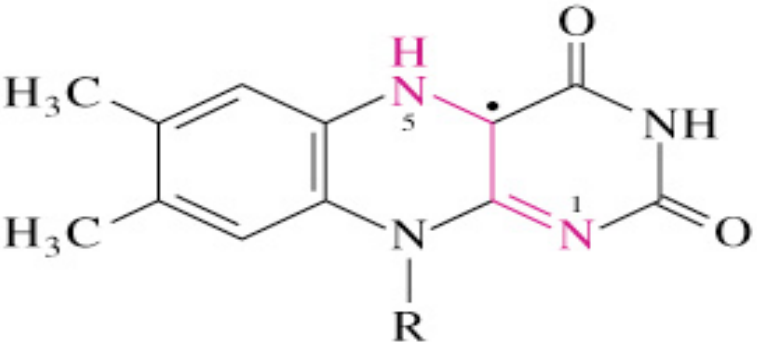






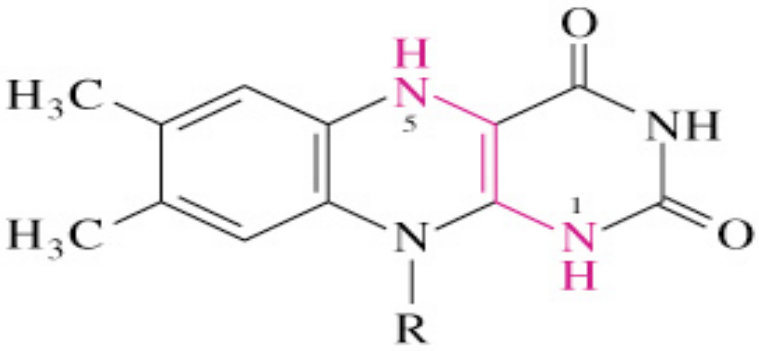
FMN or FAD
(quinone form)

$-H^{\oplus}, -e^{\ominus}$



FMNH· or FADH·
(semiquinone form)

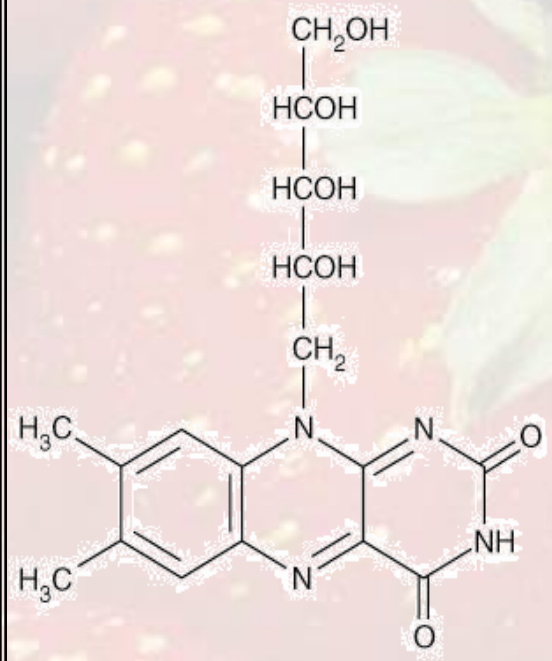
$+H^{\oplus}$
$+H^{\ominus}$



$FMNH_2$ or $FADH_2$
(hydroquinone form)

$-H^{\oplus}, -e^{\ominus}$

Flavin Coenzymes

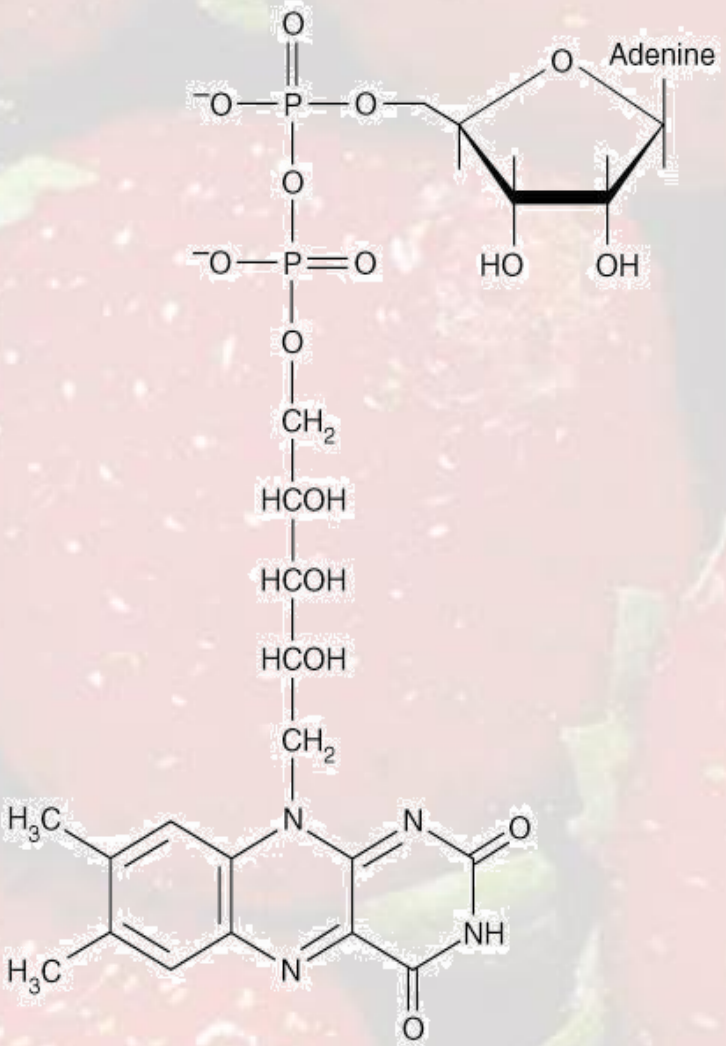


Riboflavin

(a)

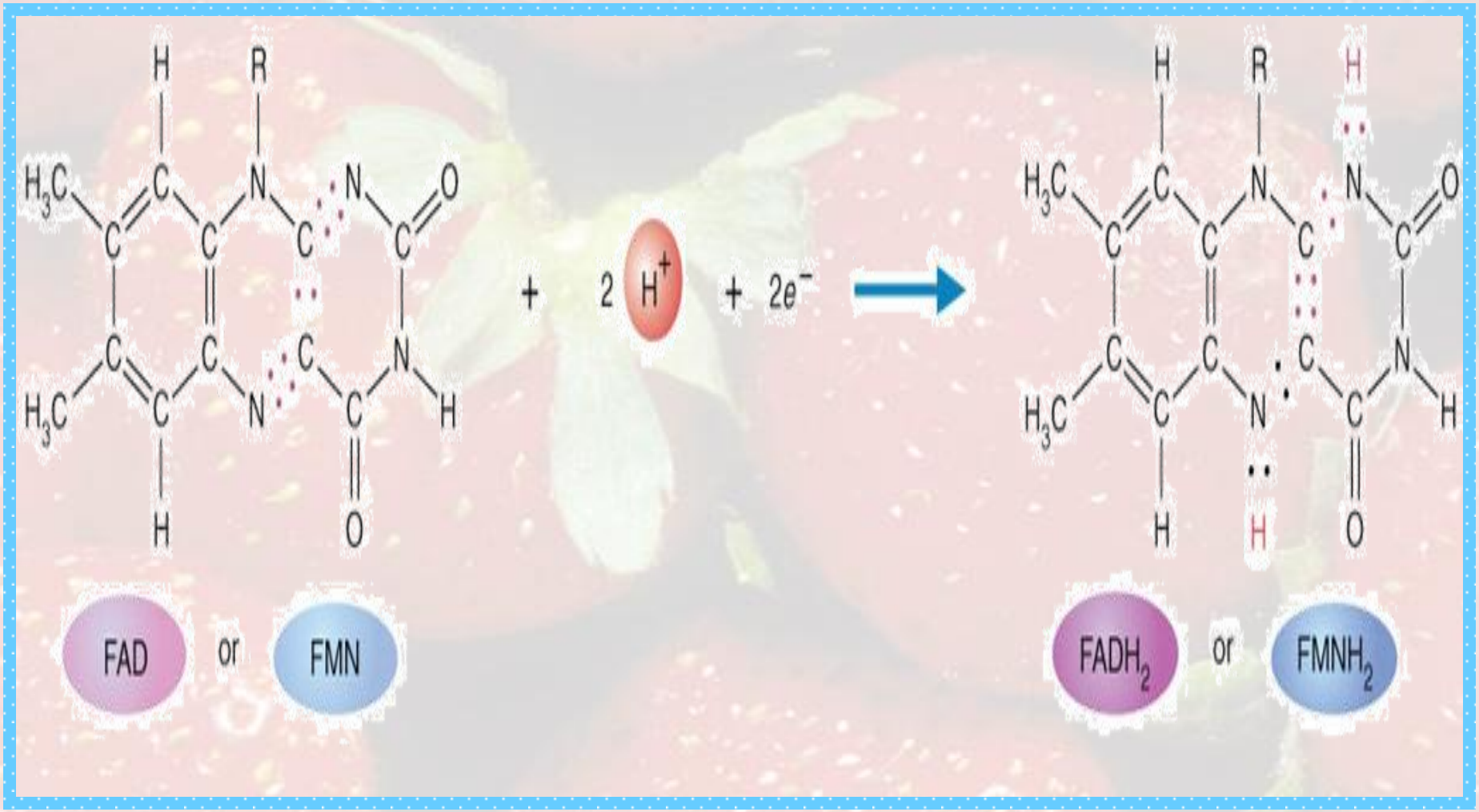
FAD

FMN

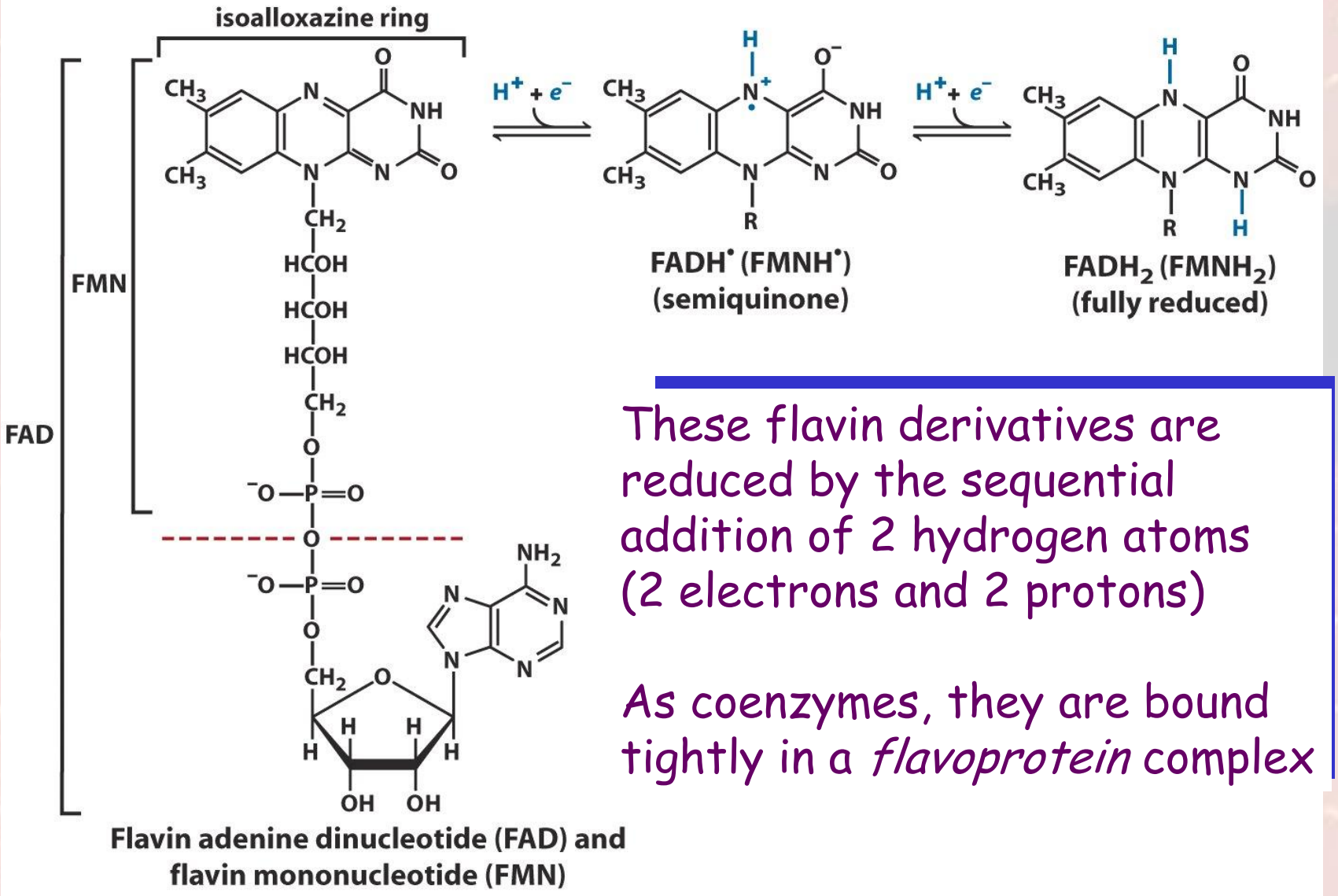


(b)

Flavin Coenzymes



$FADH_2$ and $FMNH_2$ are 2-electron carriers

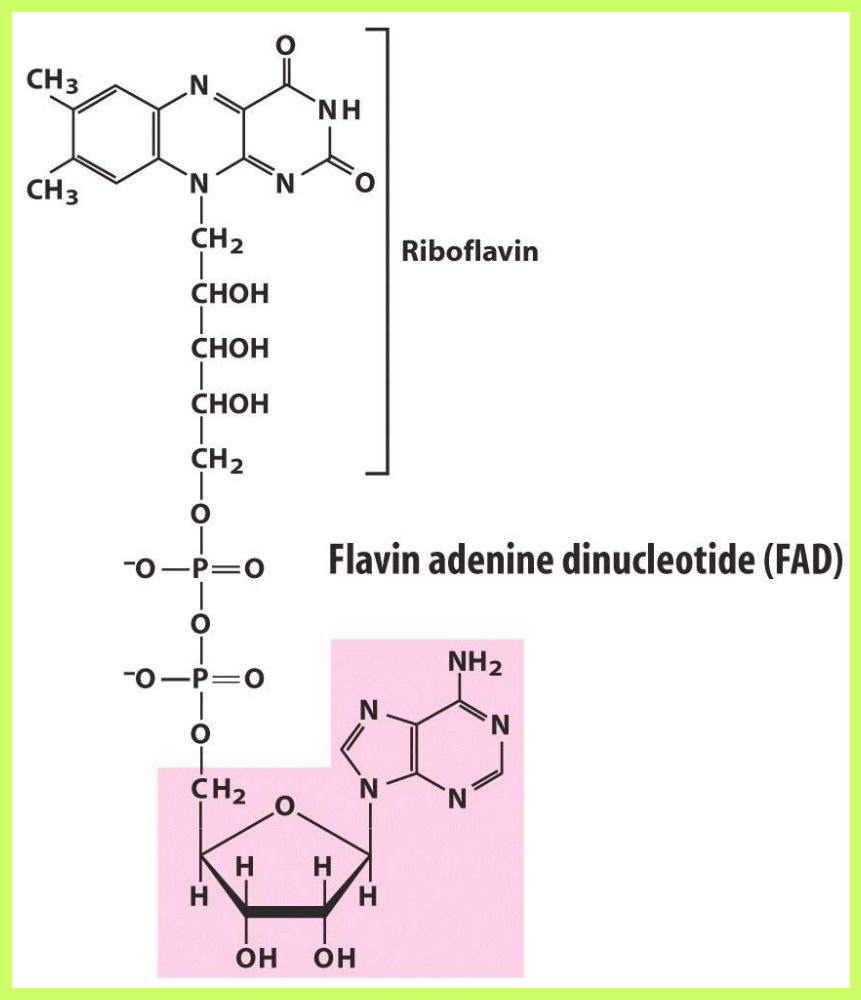


Flavin adenine dinucleotide (FAD) and flavin mononucleotide (FMN)

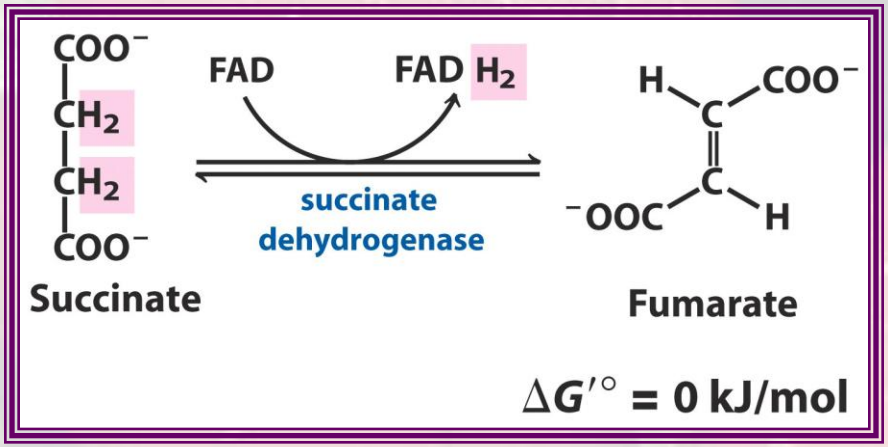
These flavin derivatives are reduced by the sequential addition of 2 hydrogen atoms (2 electrons and 2 protons)

As coenzymes, they are bound tightly in a *flavoprotein* complex

Riboflavin

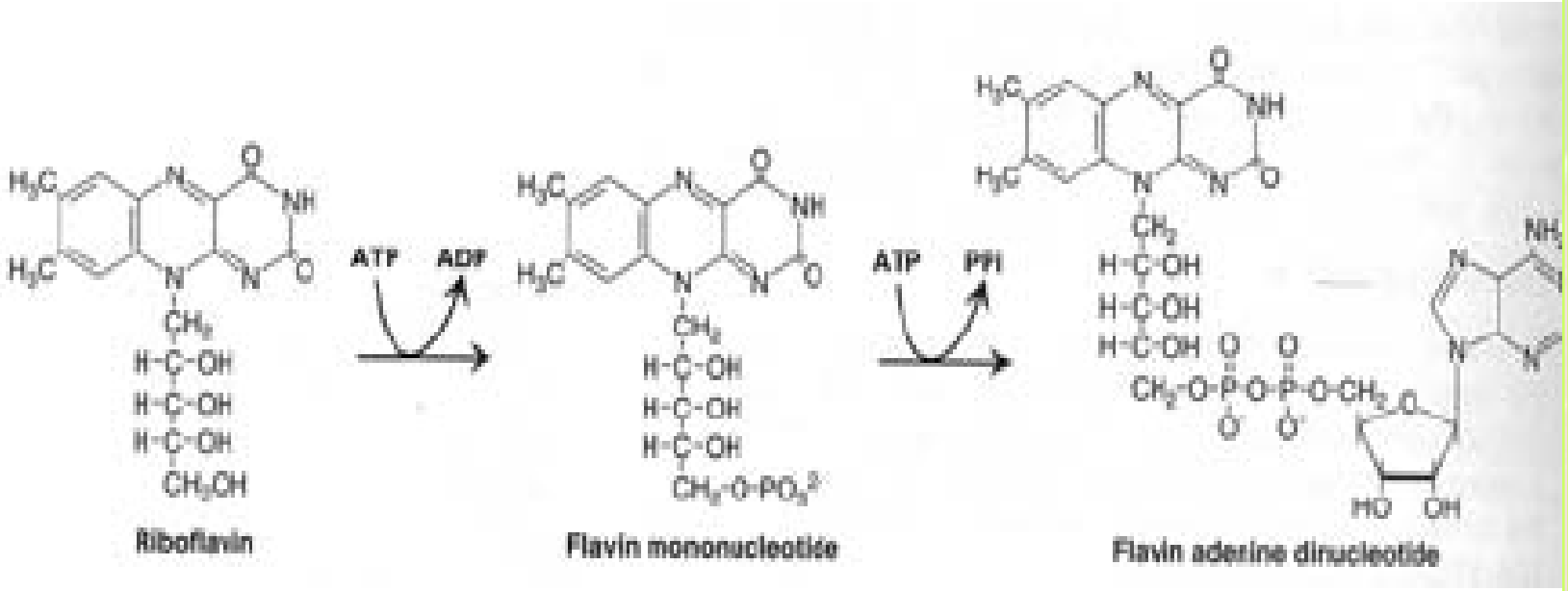


FAD is a cofactor for succinate dehydrogenase



A reaction in the citric acid cycle

FAD is made from Riboflavin or Vitamin B_2



FAD and FMN

- Flavin adenine dinucleotide (FAD) and Flavin mono-nucleotide (FMN) are derived from riboflavin (Vit B_2)
- Flavin coenzymes are involved in oxidation-reduction reactions for many enzymes (flavoenzymes or flavoproteins)
- FAD and FMN catalyze one or two electron transfers
- FAD and FMN absorb at 450 nm; $FADH_2$ and $FMNH_2$ do not. Reaction followed at 450 nm.