B-COMPLEX VITAMINS

THIAMINE (Vitamin B_1)

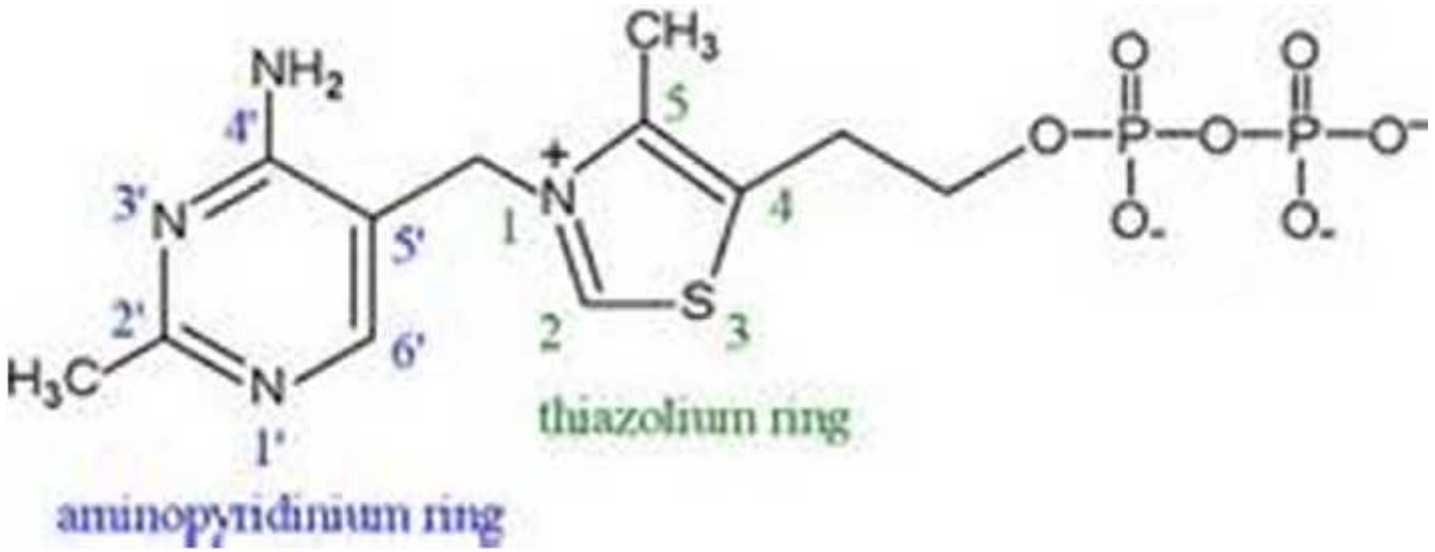
- Like other B complex vitamins, thiamine is sometimes called an "anti-stress" vitamin

- As it may strengthen the immune system and improve the body's ability to withstand stressful conditions

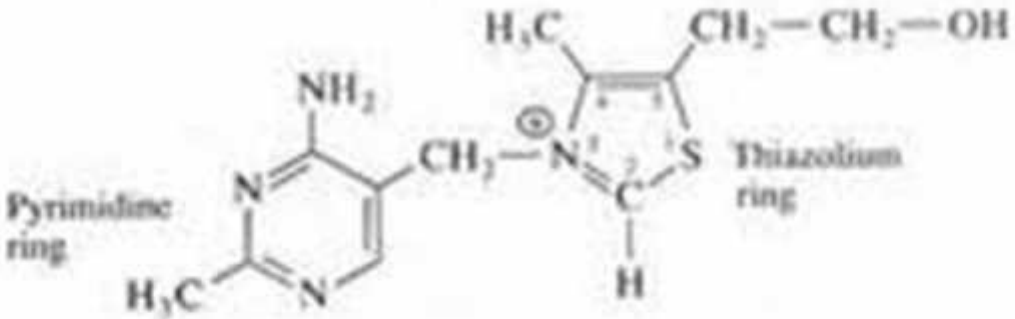
- It is named B1 because it was the first B vitamin discovered

Chemistry

- Anti beriberi factor, Anti-neurotic, aneurin
- 2 rings
- Contains S
- Free & ester (TPP) forms

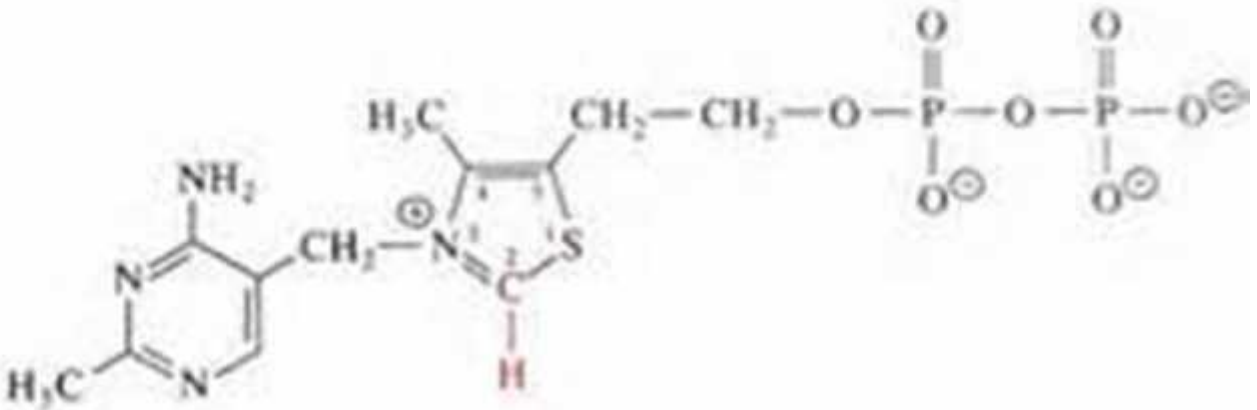


(a)



Thiamine (Vitamin B_1)

(b)



Thiamine pyrophosphate
(TPP)

- Water soluble, not soluble in fat solvents
- Resist to heat (boiling) at pH<3.5
- Lose activity > 5.5 pH
- Vegetable thiamine stable at freezing temperatures

Occurrences/sources

Plants: widely distributed

- Cereal grains- richest source
- Other sources: peas, beans, nuts, whole white bread

Animals: present in most tissues

- Liver, meat, eggs – rich sources
- Milk – low conc.

RDA

Adults

0.5 mg for 1000 calories diet

1.0 - 1.5 mg for 2000-3000 calories diet

MINIMUM: 1.0 mg

Children

0.4-1.3 mg

Biosynthesis

- Synthesized by plants, yeast, bacteria
- NOT synthesized by humans
- So required in diet
- Free form - Absorption in small intestine but not the Ester form
- Most vegetable thiamine is in free form
- TPP formed in tissues (liver, muscle, brain, RBCs)

- Present in plasma & CS fluids - free form – 1 µg/dL
- RBCs – 6-12 µg/dL as TPP
- Storage limited
- High conc. in heart, liver, kidney as free & TPP
- Low conc. in muscle, brain
- Total body thiamine – **25mg**

Excretion

- 10% excreted
- Remainder: partly phosphorylated, used as coenzymes
- Partly degraded as S compounds, inorganic SO4, excreted in urine

Metabolic Role

- **Active form – TPP**
- **Involve in Trp metabolism (tryptophan pyrrolase)**
- **Act as coenzyme (table 14-1) –Affects CH2O metabolism**

TABLE 14–1 Some TPP-Dependent Reactions

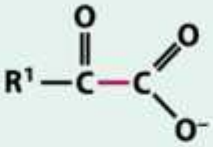
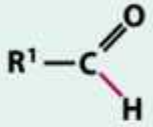
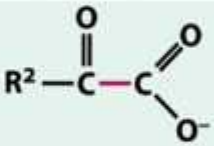
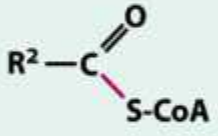
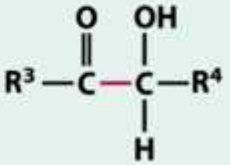
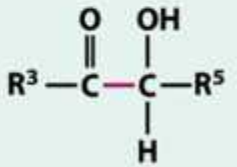
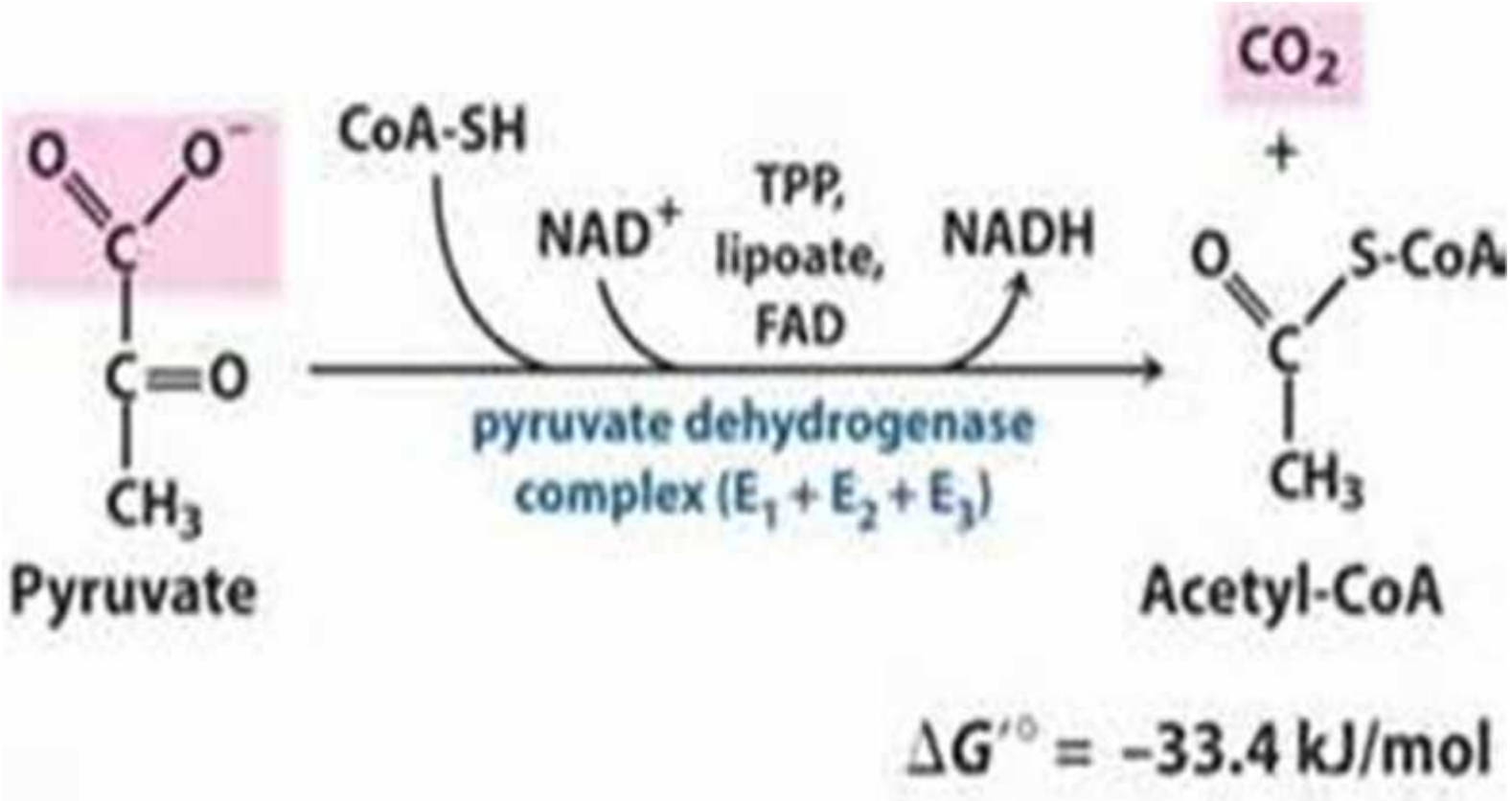
Enzyme	Pathway(s)	Bond cleaved	Bond formed
Pyruvate decarboxylase	Ethanol fermentation		
Pyruvate dehydrogenase α-Ketoglutarate dehydrogenase	Synthesis of acetyl-CoA Citric acid cycle		
Transketolase	Carbon-assimilation reactions Pentose phosphate pathway		

Table 14-1
Lehninger Principles of Biochemistry, Fifth Edition


CO2
+
CoA-SH
NAD+
TPP,
lipoate,
FAD
NADH
S-CoA
pyruvate dehydrogenase
complex (E1 + E2 + E3)
CH3
Pyruvate
Acetyl-CoA
ΔG'° = –33.4 kJ/mol

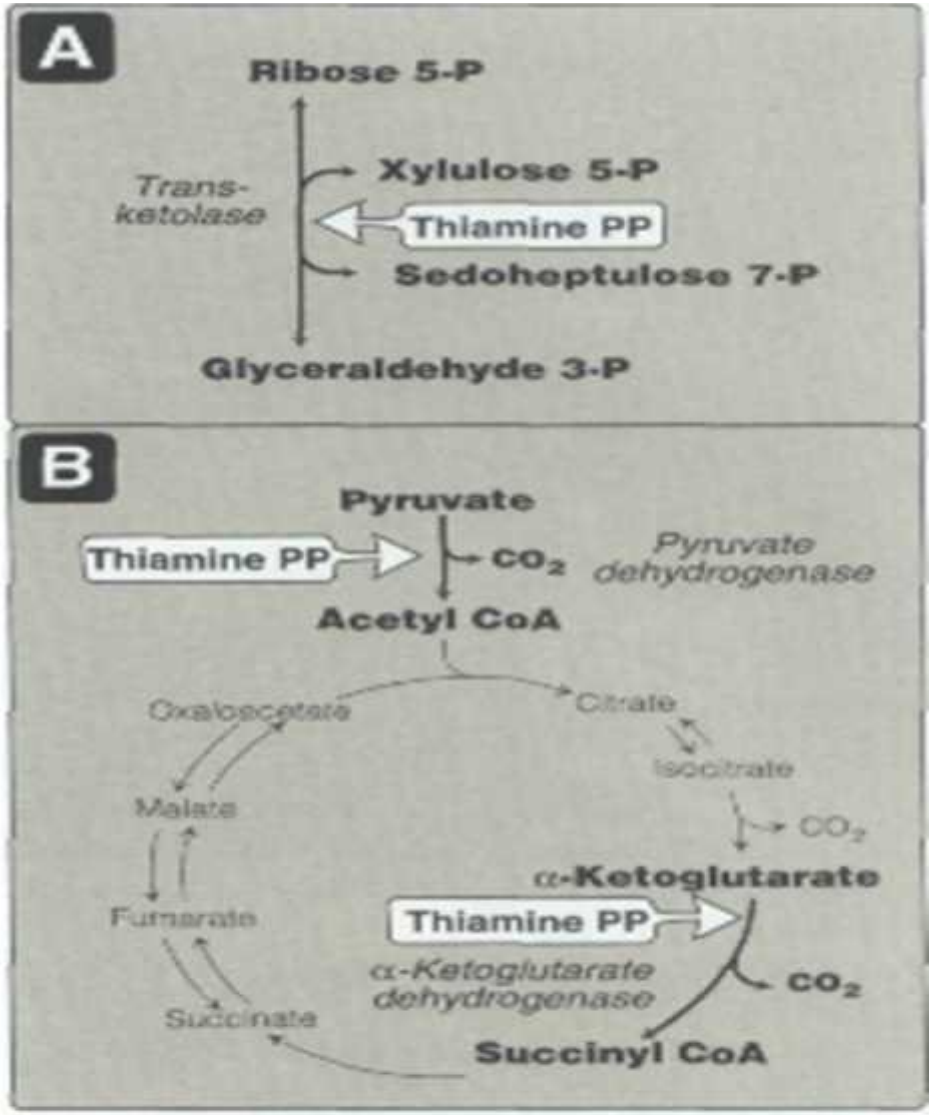
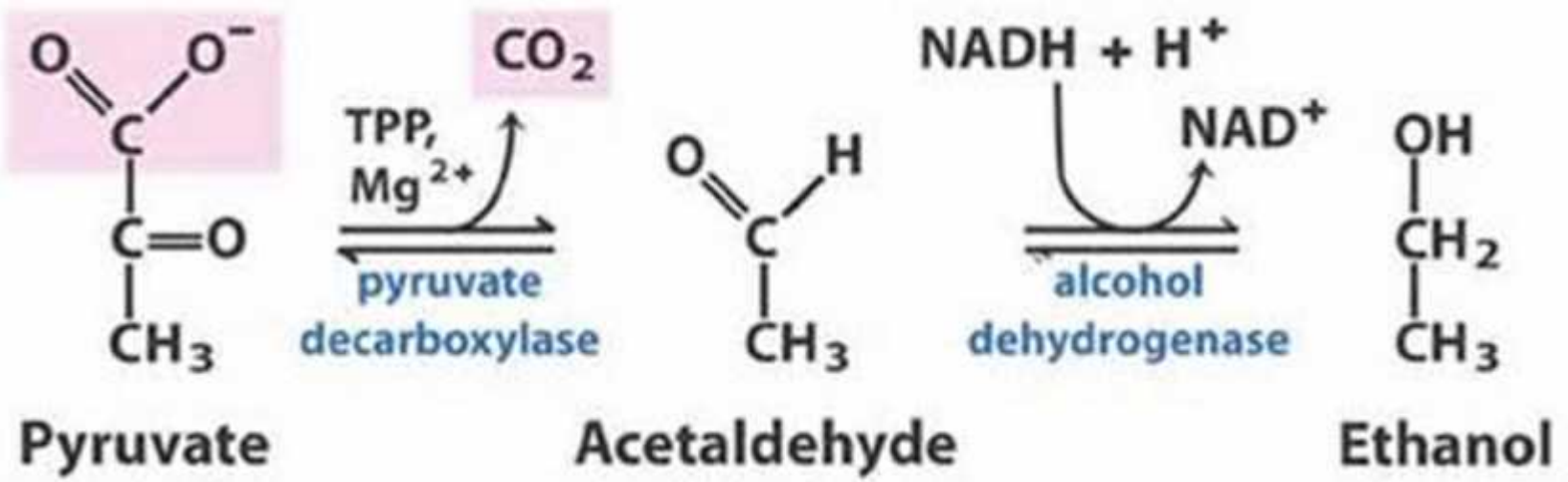


Figure 28.12
Reactions that use thiamine pyrophosphate (thiamine-PP) as coenzyme. A. *Transketolase.* B. *Pyruvate dehydrogenase* and *α-ketoglutarate dehydrogenase.*


O
O⁻
C
C=O
CH3
CO2
TPP,
Mg2+
pyruvate
decarboxylase
O
H
C
CH3
NADH + H+
NAD+
alcohol
dehydrogenase
OH
CH2
CH3
Pyruvate
Acetaldehyde
Ethanol

CLINICAL ASPECTS

Deficiency

- Beriberi: cardiac failure, polyneuritis, anorexia, , nausea, vomiting, fever
- Infantile beriberi: vomiting, convulsions, and, if not treated, death.
- Adult beriberi: dry skin, irritability, disorderly thinking, and progressive paralysis

- Oxidative decarboxylation of pyruvate & a-ketoglutarate plays a key role in energy metabolism of most cells
- Important in nervous system
- **Deficiency, the activity of these two dehydrogenase decreased**
- Decreased production of ATP
- Impaired cellular function
- Thiamine deficiency is diagnosed by an increase in erythrocyte transketolase activity observed on addition of thiamine pyrophosphate.

- Decreased Thiamine & TPP in blood & urine
- Pentose sugars accumulate in RBCs as transketolation is retarded
- Increased levels of pyruvate & lactate as oxidative decarboxylation of pyruvate is retarded
- LA/PA blood ratio disturbed – specific indicator of B1 deficiency

References:

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- Chatterjee, M. N. and R. Shinde. 2007. Textbook of Medical Biochemistry. 7th ed (Indian edition). Jaypee Brothers, Medical Publishers (P) Ltd, New Delhi, India.
- Nelson, D.L and M.M. Cox. 2013. Lehninger Principles of Biochemistry. 6th ed. Worth Publishers, NY.