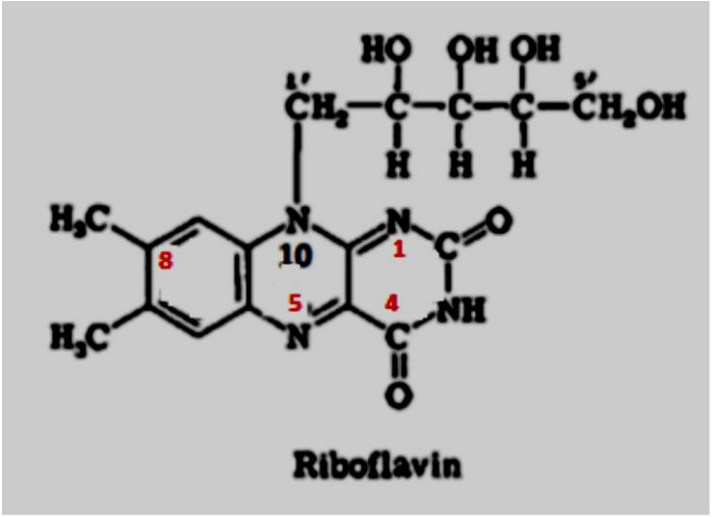
b- Vitamin B_2

(Riboflavin)

Vitamin B_2

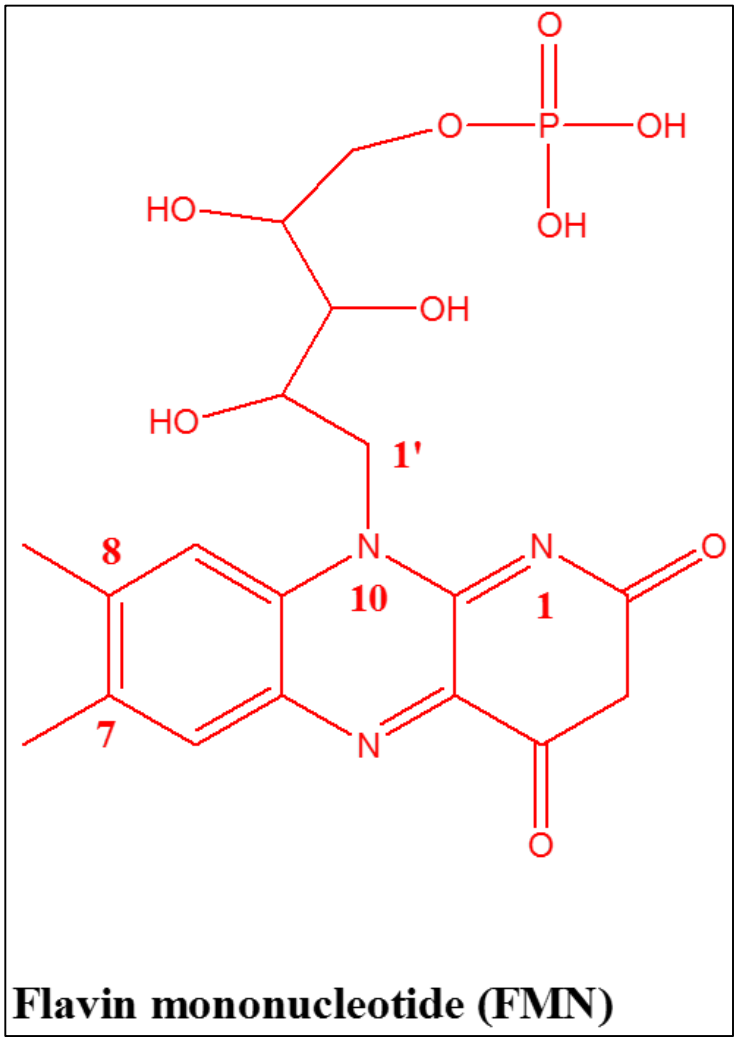
- It is called riboflavin
- It is the trivial name of the compound 7,8-dimethyl-10-(1’-D-ribityl)isoalloxazine.



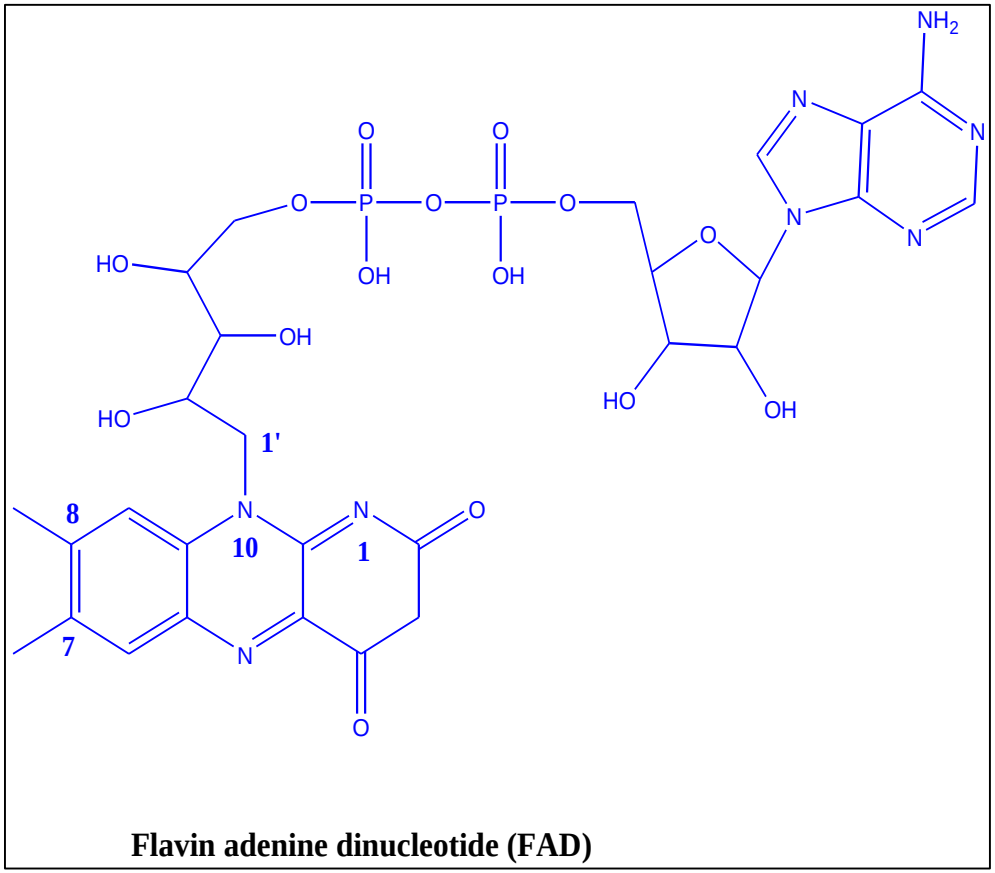
Riboflavin

Substituted isoalloxazine nucleus
D-Ribityl isde chain
Reducible nitrogen atoms in nucleus

- The metabolically active forms are Flavin mononucleotide (FMN) and Flavin adenine dinucleotide (FAD).
- FMN is not a nucleotide.
- FAD is not a dinucleotide.
- More properly, these compounds should be called Riboflavin monophosphate and Riboflavin diphosphate.



Flavin mononucleotide (FMN)



Flavin adenine dinucleotide (FAD)

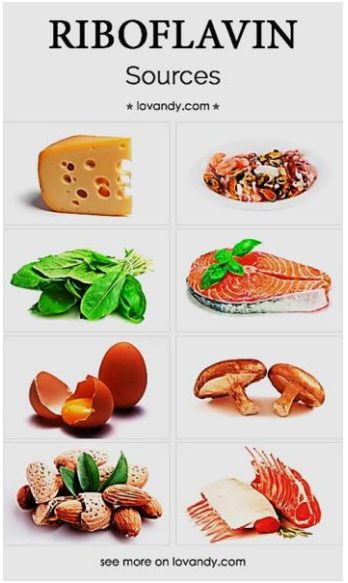
- Riboflavin is a yellow molecule that is sensitive to light and not heat.
- The catalytic functions of riboflavin are carried at positions N-1, N-5 and C-4 of the isoalloxazine nucleus.
- In addition, the methyl group at C-8 participates in covalent bonding with enzyme proteins.
- Riboflavin participates in one or two-electron redox reactions, thus serving as switching sites between obligate two-electron donors (e.g. NAD(H), succinate) and obligate one-electron acceptors (e.g. iron-sulfur proteins, heme proteins).

Significance of riboflavin

- It is essential for the intermediary metabolism of carbohydrates, amino acids and lipids.
- It also supports cellular antioxidant protection.
- It works as coenzymes (for flavoproteins) that undergo reduction through two sequential single-electron transfer steps.
- Due to this role, riboflavin deficiency will first manifests itself in tissues with rapid cellular turnover, such as skin and epithelium.

Sources of riboflavin

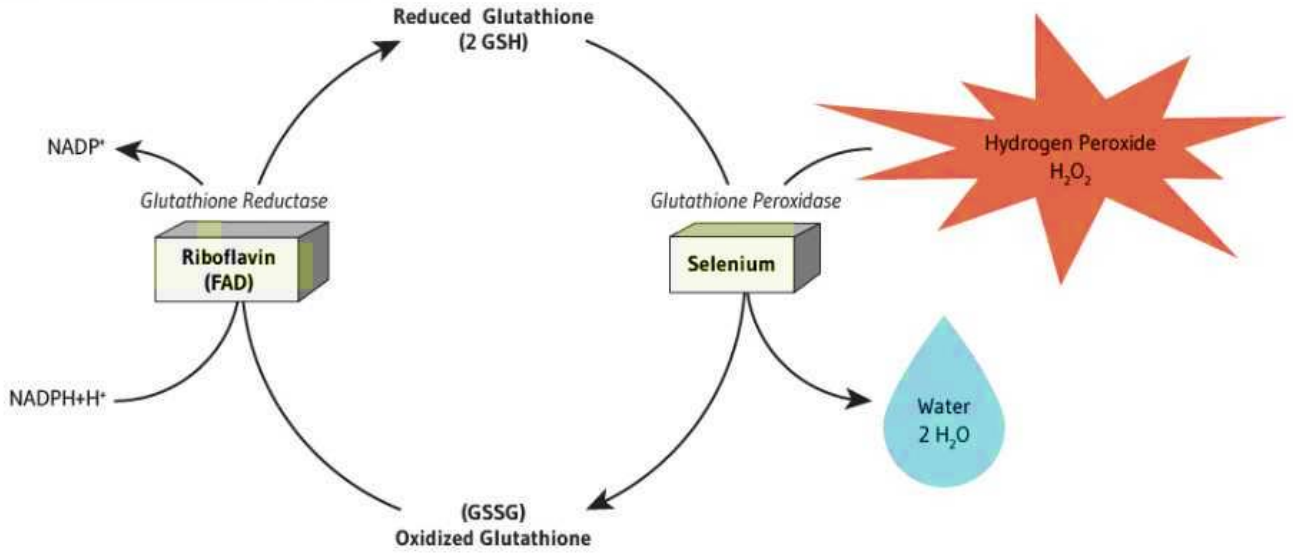
- It is widely distributed in foods as bound to proteins in the form of FMN and FAD.
- Milk, milk products, liver and eggs are good sources of the vitamin.
- It is water soluble and heat resistance.



Metabolic functions of riboflavin

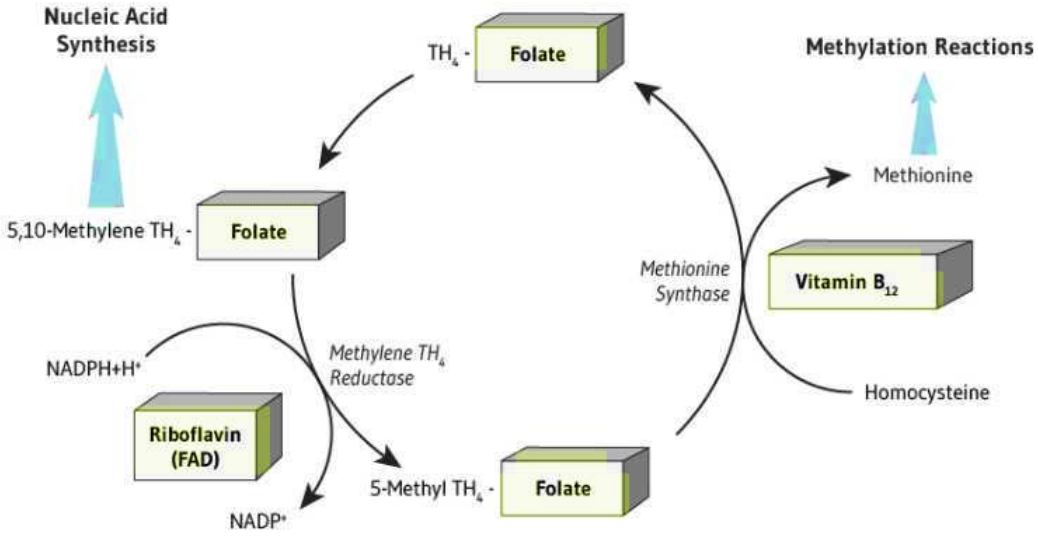
- It acts as intermediaries in transfers of electrons in biological oxidation-reduction reactions.
- It binds to many flavoproteins that include oxidases, dehydrogenases.
- These proteins are involved in either one-electron or two-electron transfers.
- So, flavoproteins serve as switching sites between obligate two-electron donors and obligate one-electron acceptors.

Figure 1. Glutathione Oxidation Reduction (Redox) Cycle

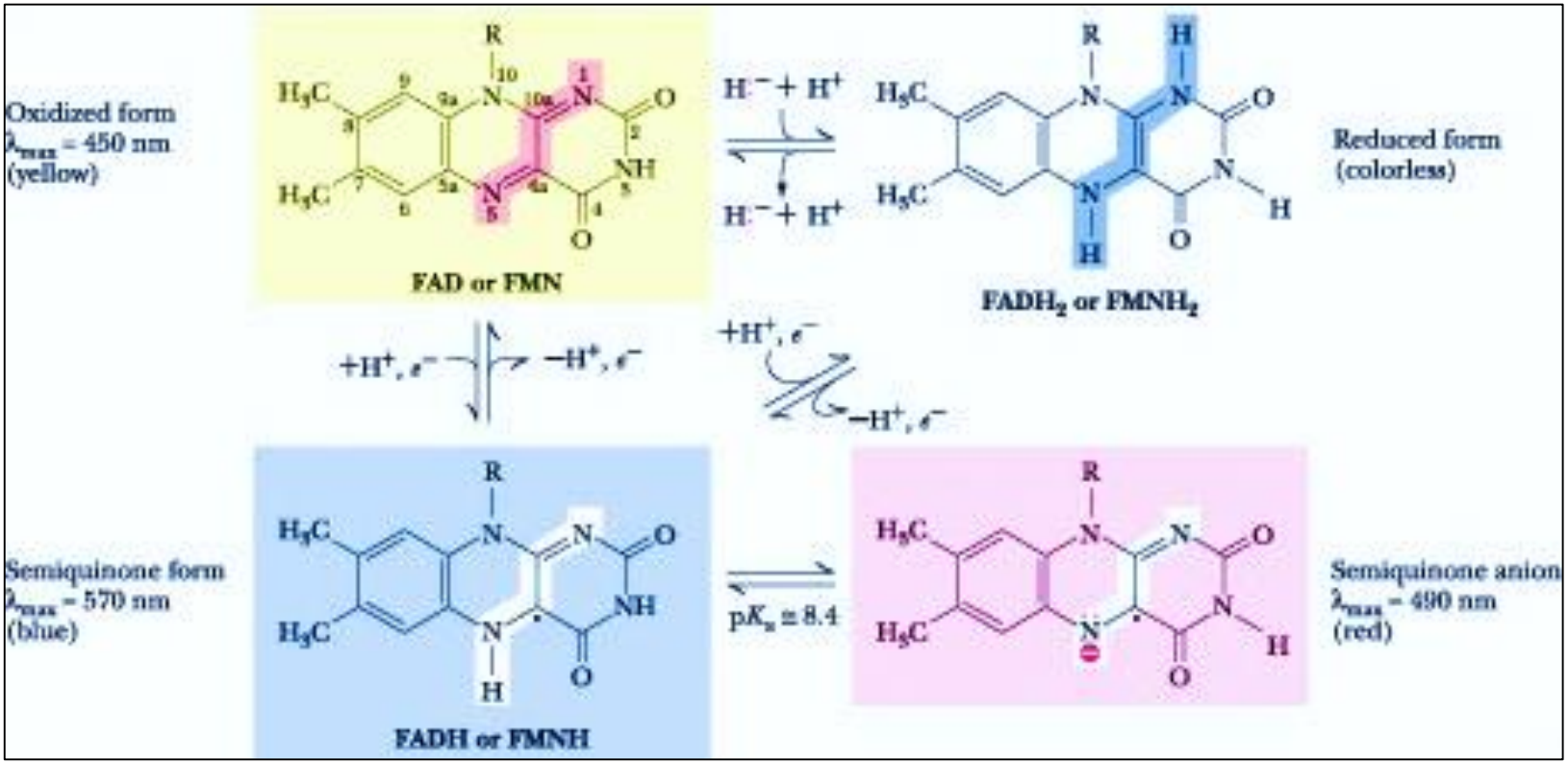


One molecule of hydrogen peroxide is reduced to two molecules of water, while two molecules of glutathione (GSH) are oxidized in a reaction catalyzed by the selenoenzyme, glutathione peroxidase. Oxidized glutathione (GSSG) may be reduced by the flavin adenine dinucleotide (FAD) dependent enzyme, glutathione reductase.

Figure 2. Folate and Nucleic Acid Metabolism



5,10-Methylene tetrahydrofolate (TH_4-folate) is required for the synthesis of nucleic acids, and 5-methyl TH_4-folate is required for the formation of methionine from homocysteine. Methionine, in the form of S-adenosylmethionine, is required for many biological methylation reactions, including DNA methylation. Methylene TH_4-folate reductase is a flavin-dependent enzyme required to catalyze the reduction of 5,10-methylene TH_4-folate to 5-methyl TH_4-folate.


Oxidized form
λ_{max} = 450 nm
(yellow)
FAD or FMN
$H^- + H^+$
$H^- + H^+$
FADH$_2$ or FMNH$_2$
Reduced form
(colorless)
$+H^+, e^-$
$-H^+, e^-$
$+H^+, e^-$
$-H^+, e^-$
Semiquinone form
λ_{max} = 570 nm
(blue)
FADH or FMNH
$pK_a \cong 8.4$
Semiquinone anion
λ_{max} = 490 nm
(red)

- Falvoproteins are involved in biological oxidations and reductions.
- They are essential for the metabolism of carbohydrates, amino acids and lipids.
- Some are essential for the activation of vitamin B_6 and B_9.
- Falvoproteins are also participate in the protection of erythrocytes and other cells from oxidative stress.

Recommended Daily Allowance (RDA)

- 1.3 mg/day to men from 14 years of age.
- 1.1 mg/day for women from 14 years of age.
- 1.4 mg/day for Pregnant women and breastfeeding.

Riboflavin deficiency

- It usually takes 3-4 months of deprivation of the vitamin to see signs of deficiency.
- These signs include cheilosis (inflammation of mouth corner), angular stomatitis, glossitis (inflammation of the tongue), hyperemia and edema of oral mucosa, dermatitis around the nose and mouth, normocytic, normochromic anemia with reticulocytopenia, leukopenia and thrombocytopenia.
- It also showed neurological signs like hyperesthesia, coldness and pain.

Factors contributing to riboflavin deficiency

1- Inadequate diet.

2- Alcoholic people.

3- Phototherapy of infants.

4- Patients receiving diuretics or undergoing hemodialysis.

Riboflavin toxicity

- It is very rare.