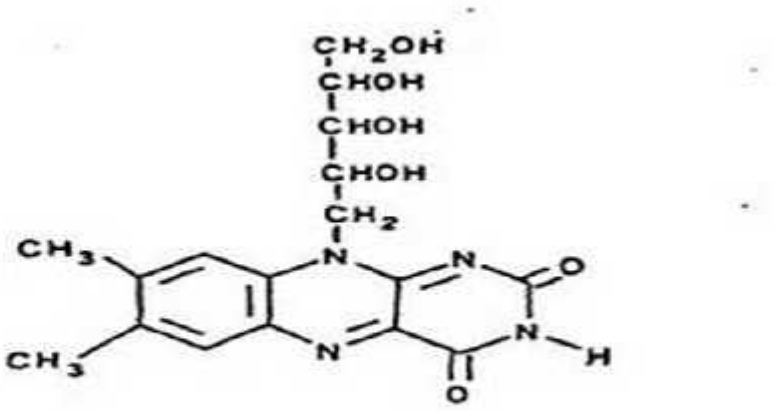
B-COMPLEX VITAMINS

RIBOFLAVIN (Vitamin B_2)

Chemistry

- Orange yellow compound
- It contains:

- A ribose alcohol (D-Ribitol: derived from ribose)
- A heterocyclic parent ring structure – Isoalloxazine – Flavin nucleus



7,8-dimethyl-10-ribityl isoalloxazine

- Biological active forms- FMN, FAD
- Both forms serve as prosthetic groups for E
- Both forms – Phosphorylated derivatives

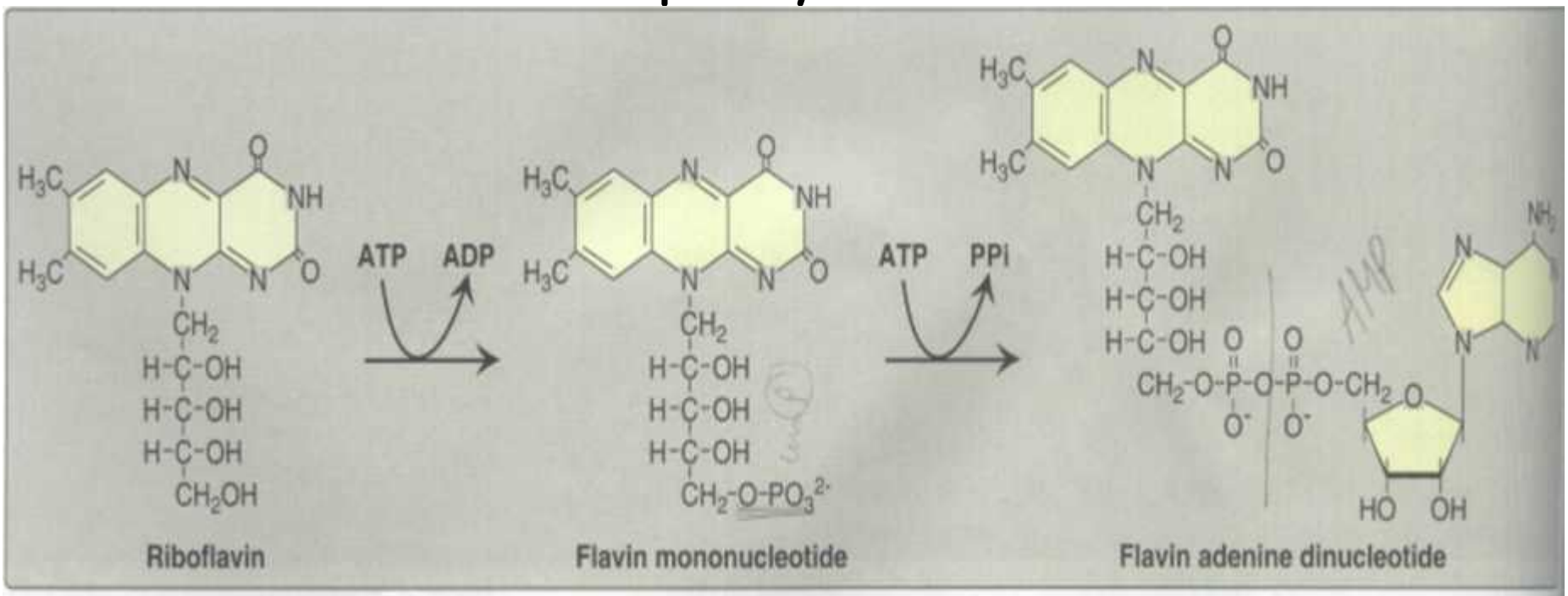


Figure 28.15
Structure and biosynthesis of flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD).

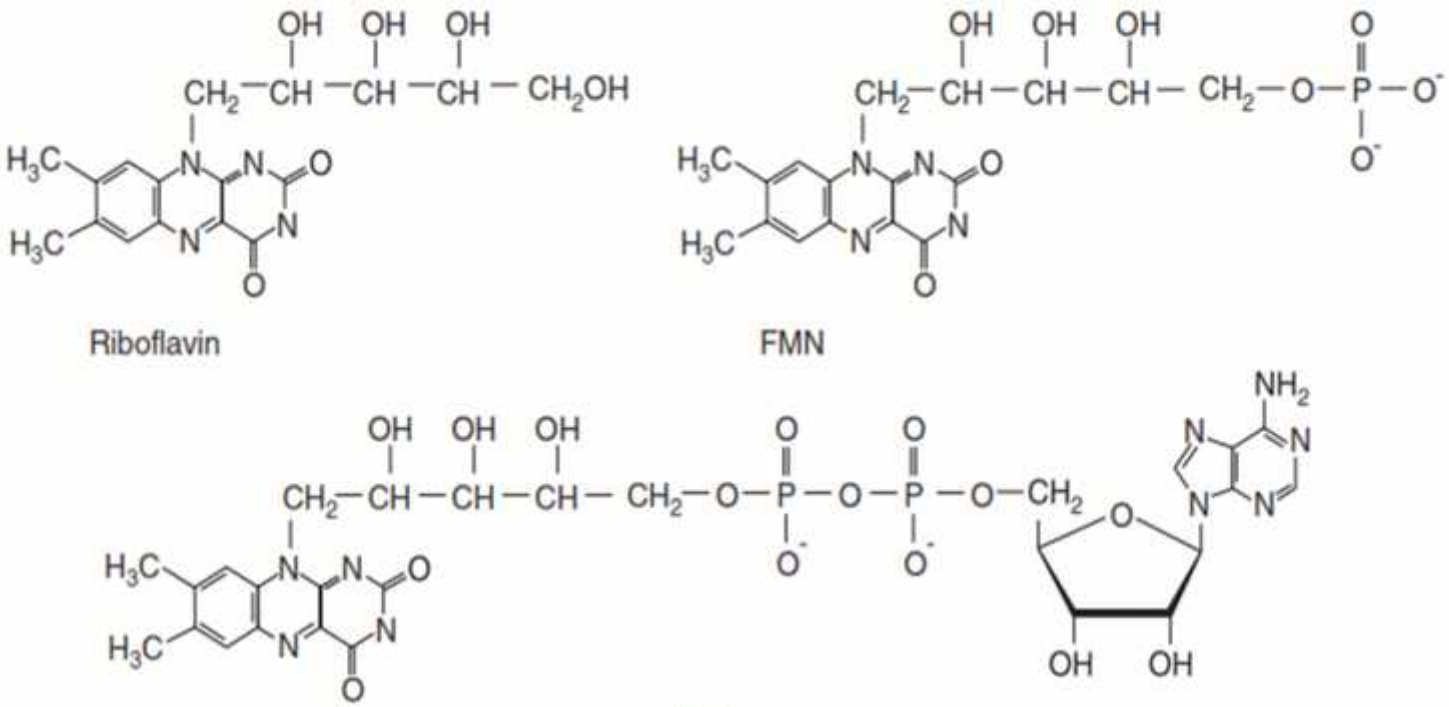


Figure 45–10. Riboflavin and the coenzymes flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD).

riboflavin

Biosynthesis

- All higher plants can synthesize it
- B_2 present as

-free form

-nucleotide form

-flavoproteins

- **Flavoproteins** contain a nucleic acid derivative of B_2 (FAD or FMN)
- Involved in a wide array of biological processes (bioluminescence, removal of radicals contributing to oxidative stress, photosynthesis, DNA repair)

- Plays a key role in energy metabolism
- Fat, carbs, protein metabolism
- Name "riboflavin" comes from Ribose; and flavin (the ring-moiety which imparts the yellow color to the oxidized molecule (from Latin *flavus*, "yellow")
- Humans & animals cannot synthesis B_2
- Dietary supply required

- Intestinal bacteria can synthesize B_2
- But quantity absorbed unable to maintain normal requirements
- Absorption: flavin nucleotides readily absorbed in small intestine
- Free B_2 undergoes phosphorylation (prerequisite for Absorption)

- Plasma levels – 2.5-4 μg (2/3 FAD, 1/3 FMN)
- RBCs – 15-30 μg/100 g
- Leucocytes, platelets - 250 μg/100 g
- These blood levels remain constant even in B_2 deficiency

Excretion

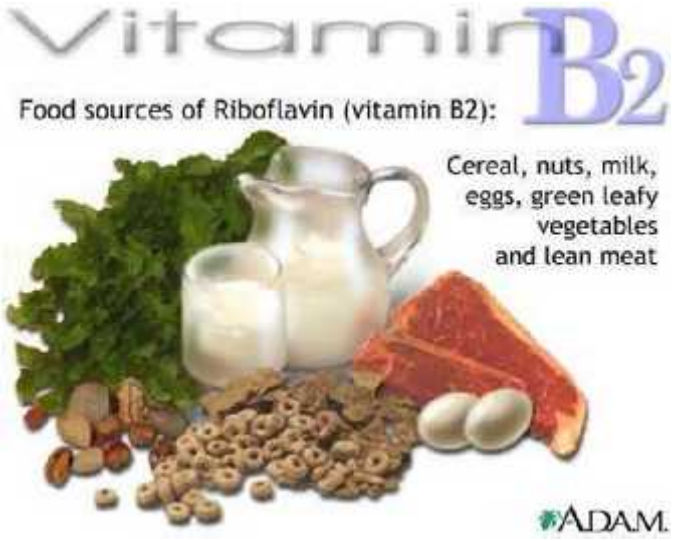
- **Urine:** mainly free (0.1-0.4 mg/day, 10-20% of intake is excreted)
- 50% as nucleotides in urine

- **Feces**: Free & nucleotide both forms
- 500-750 µg/day (large part from bacterial synthesis)

Excretion

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

Occurrences/sources



- Widely distributed
- Present in all animal & plant cells

Plants: yeast, whole grains, peas, beans, nuts, grams/DAALS, germinating seeds

Animals: Liver, kidney, eggs, milk

RDA

Exact RDA not known

Adults

1.5 – 1.8 mg

Infants/Children

0.6-1.8 mg

A solution of riboflavin

Flavin Coenzymes Are Electron Carriers in Oxidoreduction Reactions

- ETC, key enzymes in fatty acid & amino acid oxidation, citric acid cycle
- Reoxidation of the reduced flavin in oxygenases & mixed-function oxidases proceeds by formation of the flavin radical & flavin hydroperoxide with the intermediate generation of superoxide & perhydroxyl radicals, H2O2
- Flavin oxidases - a significant contribution to the total oxidant stress of the body

Metabolic roles

- Flavoproteins play role in the ETC
- FAD - Decarboxylation of pyruvate & alpha ketoglutarate
- FAD- Fatty acyl CoA dehydrogenase (fatty acid oxidation)
- FAD - production of pyridoxic acid from pyridoxal (vitamin B_6)

- Primary coenzyme form of vitamin B_6 (pyridoxal phosphate) - FMN dependent
- FAD – conversion of retinol (vit.A) to retinoic acid
- Synthesis of an active form of folate (5-methyl THF) - FADH2 dependent
- FAD – conversion of trp to niacin (vitamin B_3)
- FAD - Reduction of the oxidized form of glutathione (GSSG) to its reduced form (GSH)

- Flavoprotein enzymes - **FMN or FAD as prosthetic** groups
- FMN and FAD – tightly but not covalently bound to apoenzyme proteins
- Examples:

L-amino acid oxidase (FMN-linked enzyme in kidney (oxidative deamination of the naturally occurring L-amino acids)

- **Xanthine oxidase** (contains molybdenum & plays role in conversion of purine bases to uric acid)

- **Aldehyde dehydrogenase** (an FAD-linked enzyme in mammalian livers, which contains molybdenum & nonheme iron & acts upon aldehydes & N-heterocyclic substrates

Clinical Aspect

Deficiency

- No definite disease entity
- Riboflavin deficiency is not associated with a major human disease
- Frequently accompanies other vitamin deficiencies
- symptoms include dermatitis, cheilosis (fissuring at the corners of the mouth), glossitis (the tongue appearing smooth and purplish)

References:

- Champe, P.C., R.A. Harvey and D.R. Ferrier. 2008. Biochemistry: Lippincott's Illustrated Reviews . 4th ed. Lippincott Williams and Wilkins. U.S.A.
- Chatterjee, M. N. and R. Shinde. 2007. Textbook of Medical Biochemistry. 7th ed (Indian edition). Jaypee Brothers, Medical Publishers (P) Ltd, New Delhi, India.
- Murray, R.K., D.A. Bender, K. M. Botham , P.J. Kennelly,V.W. Rodwell and P.A.Weil. 2009. Harper's Illustrated Biochemistry. 28th ed. McGraw Hill. New York.