Riboflavin was the first B-complex vitamin to be isolated in a pure state.

1931: Warburg showed that this substance was essential for cellular respiration.

Alex Throell isolated the vitamin.

1935: Paul Karrer elucidated the structure.

- Nobel Prize in 1937.
Chemistry

- Riboflavin contains a 3-ring heterocyclic parent structure ‘Isoalloxazine’ nucleus (Flavin nucleus)
- To this 6,7-dimethyl - isoalloxazine ring Carbon 1 of ribose alcohol ‘D-ribitol’ is attached at its 9th position
- Ribitol has an open chain structure
- Riboflavin is a heat stable, water-soluble orange-yellow compound
- Solution of riboflavin when exposed to UV light, it is converted in to ‘lumiflavin’ which emits a strong greenish-yellow fluorescence
- Riboflavin exists in the form of Lactoflavin (milk), Hepatoflavin (liver), Ovoflavin (eggs) & Verdoflavin (grass)
Sources

- Rich Sources: Yeast, whole grains, legumes, nuts, green vegetables & germinating seeds
- Good Sources: Liver, kidney, crab meat, fish, milk & eggs
- Intestinal flora also synthesise riboflavin
**Recommended Dietary Allowance**

- **Adults:** 1.5 to 1.8 mg/day
- **Infants & Children:** 0.6 to 1.5 mg/day
- **Pregnancy, Lactation & Elderly:** 1.8 to 2.5 mg/day
- **RDA is dependent on calorie intake**
Absorption, Storage, Transport & Excretion

- Riboflavin is readily absorbed from the small intestine.
- It is transported all the tissues by general circulation.
- Riboflavin exists in tissues as tightly bound with enzymes.
- Excess riboflavin is not stored in the body.
- Major part is excreted as such in urine and a small part is broken down in the tissues.
- Normal serum riboflavin levels is 2.5 - 4 μg/dl.
Functions

Biologically active coenzyme forms of riboflavin are –
- Flavin Mono-Nucleotide (FMN)
- Flavin Adenine Dinucleotide (FAD)

FMN – Phosphoric acid is attached to ribityl alcoholic group at position 5, synthesised by ‘Flavokinase’ requiring ATP

FAD – Ribityl alcoholic group in position 5 is linked to an adenine nucleotide through pyrophosphate linkage, synthesised from FMN by ‘FAD synthase’ requiring ATP

Phosphoric acid group has the capacity of combining with protein apoenzyme forming ‘Flavoproteins’ (Holoenzyme)

Flavoproteins may also combine with metals like iron & molybdenum forming ‘Metalloflavoproteins’
Functions (Contd)

FMN & FAD act as co-enzymes in various Hydrogen-transfer reactions

- During oxidation-reduction process, two hydrogen atoms from substrate are accepted by each molecule of FMN/FAD, which in turn gets reduced to FMNH$_2$/FADH$_2$

- The sites where the two hydrogen atoms gets attached are same in both FMN & FAD – two nitrogen atoms at position 1 & position 10 of isoalloxine nucleus
Functions (Contd)

Principle enzyme reactions catalysed by FMN & FAD are as follows:

- **FMN – dependent enzymes**
  - (a) L-aminoacid oxidase
    - Involved in oxidation of L-amino acid to \( \alpha \)-ketoacid & ammonia
  - (b) Cytochrome-c-reductase
    - Component of Complex III of electron transport chain
  - (c) NADH dehydrogenase
    - Component of Complex I of electron transport chain
Functions (Contd)

FAD – dependent enzymes

(a) D-aminoacid oxidase
- Involved in oxidation of D-amino acid to α - ketoacid & ammonia

(b) Xanthine oxidase
- Involved in conversion of Xanthine to hypoxanthine in Purine metabolism

(c) Succinate dehydrogenase
- Conversion of succinate to fumarate in TCA cycle
Functions (Contd)

✓ FAD – dependent enzymes

(d) Glycine oxidase
- Cleavage of Glycine to Glyoxylate & ammonia

(e) Acyl CoA dehydrogenase
- Conversion of acylCoA to $\alpha,\beta$ Unsaturated acyl CoA

(f) Dihydrolipoate dehydrogenase
- Conversion of Pyruvate to Acetyl CoA in pyruvate dehydrogenase complex reaction
- Conversion of $\alpha$-ketoglutarate to succinyl CoA in $\alpha$-ketoglutarate dehydrogenase complex reaction
Deficiency Manifestations

- Natural deficiency of riboflavin alone is not common
- Riboflavin deficiency is manifested along with other B-complex vitamin deficiency & kwashiorkar
- Deficiency manifestations are confined to skin & mucous membranes
- Symptoms: Glossitis, Megenta tongue, Cheliosis, Angular stomatitis, Atrophy of lingual papillae, Corneal vascularisation & Seborric dermatitis
- Assay of ‘Glutathione reductase’ activity in RBCs – useful in assessing riboflavin deficiency
- Prompt administration of riboflavin along with other B-complex group of vitamins will reverse the symptoms