RIBOFLAVIN CHEMICAL STRUCTURE AND ITS SOURCES

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ABSTRACT

Riboflavin also called Vitamin B2, is one of the 8 B vitamins. All B vitamins help the body convert food (carbohydrates) into fuel (glucose), which is used for energy production. These B vitamins, often referred to as B vitamins, also help the body absorb fats and proteins.Riboflavin is essential for maintenance of the skin, the mucous membranes, the cornea of the eye, and nervous system structures such as the myelin sheaths that surround the nerves. In experimental animals, development of the fetus and resistance to infections are impaired by deficiency of this vitamin. Riboflavin is part key of two important coenzymes called flavin mono nucleotide or (FMN) and flavin adenine dinucleotide (FAD).These coenzymes are involved in complex oxidation-reduction conversions in the liver, electron transport mechanisms that release energy within cells, and other important cellular respiratory functions.

Keywords: VitaminB2, Riboflavin, FMN, FAD, Coenzyme, water soluble

1. **Discovery of Riboflavin**
2. **Introduction and History of Riboflavin or VitaminB2**

The first description of what was later identified as a case of riboflavin deficiency was by Stannus in 1912 in the British Journal of Tropical Medicine. In 1938, Americans Sebren and Butler published the first definitive report on riboflavin deficiency in humans, which became known as ariboflavinosis. these and subsequent reports picture victims as suffering from inflammations of the eyes, lips, mouth and tongue, as well as scaly, greasy skin eruptions (seborrheic

dermatitis).Much further understanding of riboflavin's role in human nutrition was contributed in 1949 by a reasearch group led by M. K. Horwitt.[1] Preparing pure riboflavin seemed at first to be an impossible job.

Water extracts of vegetable or grain sources turned out to be mixtures of three water soluble B vitamins, thiamin, riboflavin and small amounts of niacin.the fact that some symptoms of riboflavin deficiency are similar to those of pellagra created additional confusion.Finally, the research team of Kuhn, Gyorgy and Wagner Jauregg in 1933 isolated pure riboflavin from milk and proved it was different from thiamin and niacin. The molecule consists of a d-Ribitol unit attached to an isoalloxazine ring (Figure3-1). Anything more than a minor change in the molecule results in a loss of vitamin activity. Aqueous solutions of riboflavin are yellow with a yellowish green fluorescence. The vitamin is a constituent of two coenzymes or The two biologically active forms are flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD) [2], In the pioneering studies by McCollum and Kennedy (3) in the early part of the twentieth century, water-soluble tissue extracts were found to be effective in the prevention of the deficiency state of pellagra in experimental animals. As studies progressed, it became evident that there were at least two distinct fractions of these extracts, one of which was heat-labile and the other heat-stable. Further studies of this heat-stable fraction showed that it was a complex containing a yellow growth factor. This factor had fluorescent properties and was later purified and named riboflavin (B2) (4). Other components of this fraction were later identified as niacin, which was the true antipellagra compound, and vitamin B6, which was particularly effective in preventing dermatitis in animals. The physiological role of the yellow growth factor remained obscure until the land-mark discovery by Warburg and Christian (5) in 1932 of ‘‘yellow enzyme’’ or ‘‘old yellow enzyme.’’ This protein was found to be composed of an apoenzyme and a yellow co-factor serving as a coenzyme. This coenzyme was shown subsequently to contain an isoal-loxazine ring (6) and a phosphate group (7). Synthesis of riboflavin was accomplished by Kuhn et al. (8) and Karrer et al. (9). The flavin coenzyme riboflavin-5′-phosphate (flavin mononucleotide, FMN), was identi-fied in 1937 by Theorell (10). In 1938, Warburg and Christian (11) clarified the structure of flavin adenine dinucleotide (FAD), formed from FMN. While many enzymes utilize FMN and FAD as cofactors, flavins bound covalently to specific tissue flavoproteins also have been found to have major biological significance, as reviewed by Mc Cormick(12).determination of riboflavin's exact chemical structure

and its synthesis in pure form were achieved in 1935 by two independent groups,a German group led by Richard Kuhn and a Swiss group headed by Paul Karrer. Dr. Karrer received a Nobel Prize in 1937, and Dr. Kuhn was awarded one the following year. However, because Kuhn was Jewish and had just been placed in a Nazi concentration camp, Hitler refused to let him accept. Surviving the war and the Nazis, Dr.Kuhn finally was formally honored by the Nobel Prize Committee [13].

3. chemical structure and biological role

Riboflavin structure Formula figure 3-1, is the prosthetic group of flavine enzymes, which are of great importance in general metabolism and particularly in metabolism of protein.

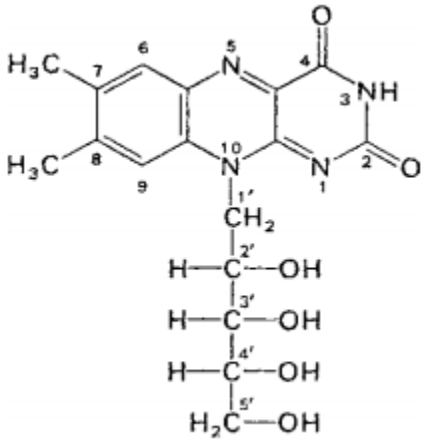

Figure 3-1. Chemical structure of VitaminB2 or riboflavin

Riboflavin, formerly known as vitamin B2, is the generic term for the group of compounds that exhibit the biological activity of riboflavin Figure 3-2, The parent compound of the riboflavin family is7,8 dimethyl- 10(1-D-ribityl) isoalloxazine compound, and all derivatives of riboflavin are given the generic name flavins. Phosphorylation of the 5'-position of the ribityl side chain yields flavin mononucleotide (FMN), whereas flavin adenine dinucleotide (FAD) has an additional 5'- adenosyl monophosphate moiety Figure 3-2. FMN and FAD function as conezymes in a large number of flavin-dependent enzymes that catalyze various oxidation-reduction processes. Both forms are readily convertible to riboflavin by action of phosphatases that are present in foods and those of the digestive system. A relatively minor (< 10%)

of the FAD in biological materials exists in a covalently bound enzyme form in which position 8a is covalently linked to an amino acid residue of the enzyme protein.

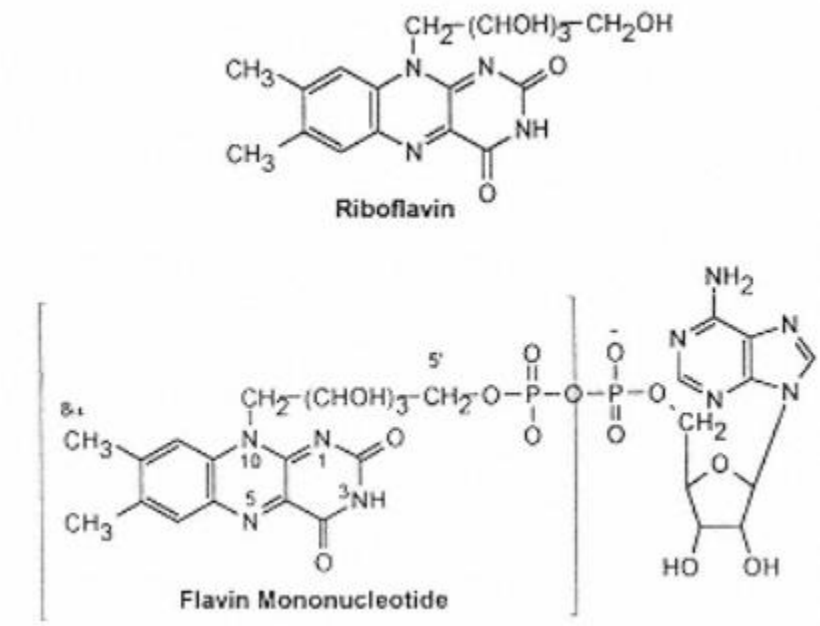

Figure 3-2 structures of riboflavin, flavin mononucleotide, & flavin adenine dinucleotide.

4. Stability

Riboflavin is relatively stable in normal food handling prapare .losses range from 10–15% .Exposure to light, particularly in the visible spectrum from 420–560 nm. Photolytically cleaves ribitol from the vitamin, exchanging it to lumilactoflavin. Lumiflavin is toxic product of riboflavin.[14].

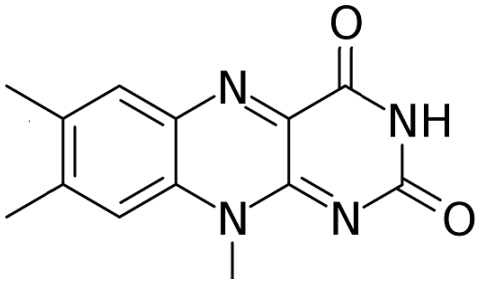

Figure 4-3. Chemical structure of Lumiflavin[14]

Also Riboflavin exhibits its greatest stability in acidic medium, is somewhat less stable at neutral pH, and rapidly degrades in alkaline

environments. Retention of riboflavin in most foods is moderate.[15].

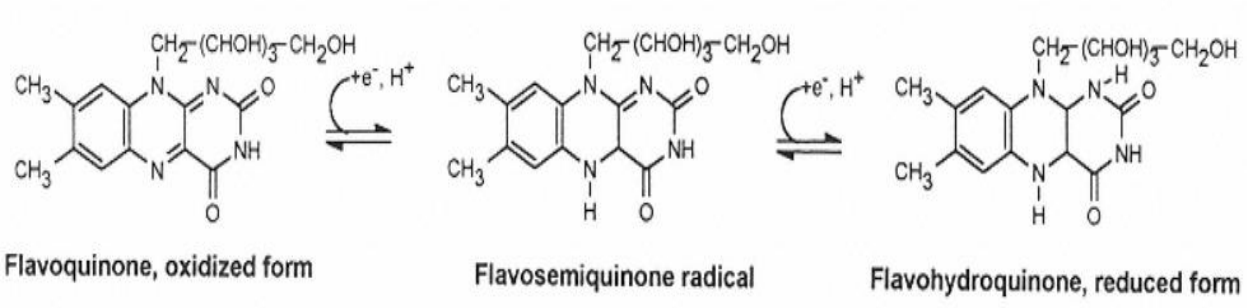

Figure 4-4.Oxidation - reduction behavior of flavins.

To very good during conventional thermal processing, handling, and preparation. Losses during storage of riboflavin in various dehydrated food systems breakfast cereals and model systems are usually negligible. Rates of degradation increase measurably at aw above the monolayer value when temperatures are above ambient. [16].

5. How Much lbooflavin Do People Need? (Requirement)

The human requirement for riboflavin varies with metabolic activity and body weight and ranges from 1 to 3 mg per day. Normal adult requirement is 1.1mg to 1.6 mg per day. In most cases, the riboflavin of foods is present in the form of the dinucleotide, the phosphoric acid ester, or is bound to protein. Only in milk does riboflavin occur mostly in the free form.[2].

Also Recommended Dietary Allowance is 1.3 mg for young women and 1.7 mg for young men.When 2 to 3 times this amount is ingested, the excess is rapidly excreted in the urine, giving it a bright yellow color. In the United States, riboflavin deficiency requiring therapy occurs mainly in severe malnutrition such as is found in alcoholics.[13].

6. Food Sources of Riboflavin

The richest sources of vitaminB2 (riboflavin) are milk and other dairy products the organ meats kidney and liver of cows, pigs and chickens and also yeast. As with thiamin, moderate amounts of vitaminB2 are found in most fruits, vegetables, grains, lean meats and poultry. According to Professor George Briggs, milk supplies nearly 40 percent of the vitaminB2 in

the American diet. Important amounts are also supplied by enriched bread and cereals. [13].

Table 6-1. Riboflavin Content of Some Foods [2].

Number	Product	VitaminB2 Mg/100Edible potion
1	Beef	0.16
2	Cabbage	0.05
3	Eggs	0.30
4	Chicken	0.19
5	Beef Liver	3.26
6	Chicken Liver	2.49
7	Beef Kidney	2.55
8	Peas	0.29
9	Spinach	0.20
10	Tomato	0.04
11	Yeast (Dry)	5.41
12	Milk	0.17
13	Nonfat dry milk	1.78

The light sensitivity of riboflavin results in losses of up to 50 percent when milk is exposed to sunlight for two hours. The nature of the packaging material significantly affects the extent of riboflavin destruction. Itappears that the wavelengths of light responsible for the riboflavin destruction are in the visible spectrum below 500 to 520 nm. Ultra-violet light has been reported to have no destructive effect on riboflavin (17). Riboflavin is stable in dry milk for storage periods of up to 16 months. Pasteurization of milk causes only minor losses of riboflavin. [18].

7. Toxicity Humans body

Vitamin B2 or Riboflavin has always been considered safe for humans or animals at any oral dosage and no cases of toxicity have been reported. According to Horwitt[19],1,000 mg orally per pound of body weight has produced no ill effects in animals.

T. K.Basu[20], reported on animal studies in which high dosages of riboflavin could retard some malignant tumors but increased the growth of others.

8. Functions

The major function of riboflavin, as noted above, is to serve as the precursor of the flavin coenzymes, FMN and FAD and of covalently bound flavins. These coenzymes are widely distributed in intermediary metabolism and catalyze numerous oxidation–reduction reactions. Because FAD is part of the respiratory chain, riboflavin is central to energy production. Other major functions of riboflavin include drug and steroid metabolism, in conjunction with the cytochrome P450 enzymes, and lipid metabolism. The redox functions of flavin coenzymes include both one-electron transfers and two-electron transfers from substrate to the flavin coenzyme [15]. Flavoproteins catalyze dehydrogenation reactions as well as hydroxylations, oxidative decarboxylations, dioxygenations, and reductions of oxygen to hydrogen peroxide.Thus, many different kinds of oxidative and reductive reactions are catalyzed by flavoproteins.[15].

9. Deficiency of Riboflavin

No pathologically severe symptoms attributed to vitamin B2 deficiency have been observed in humans. Deficiency symptoms have been induced experimentally in volunteers whose diets were lacking only in the vitamin or who were fed vitamin B2 antagonists. Symptoms usually include lesions of the lips (cheilo-sis) and angles of the mouth (angular stomatitis), a fissured and magenta coloured tongue (glossitis), seborrhoeic follicular keratosis of the nose and fore head, and dermatitis of the anogenital region. Ophthalmic symptoms are a superficial vascularization of the cornea accompanied by intense photophobia [21].

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