Riboflavin

What We Know

› Riboflavin (also known as vitamin B2, lactoflavin, and vitamin G) is a water-soluble, B-complex vitamin. Riboflavin is an essential micronutrient that should be replenished daily to avoid depletion; which is not difficult because it is present in a wide variety of foods, is included in fortified food programs, and is easily absorbed from the upper gastrointestinal tract (GI) tract. As a result, riboflavin deficiency is rare for uncompromised individuals in Western countries (5,6,11,13,14,18).

  • Although a small amount of riboflavin in food occurs in the free form, about 90% is present in the noncovalently-bound forms of flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD) (2,6,10,11,13,14).

› Actions of riboflavin (2,5,6,10,11,12,13,14,18)

  • The coenzymes FMN and FAD are biologically active forms of riboflavin
  • FMD and FAD function as electron carriers
  • Riboflavin catalyzes proteins involved in respiratory reactions to produce energy
  • The coenzymes contribute to the formation of vitamins B6, B12, and niacin (also called vitamin B3) and their coenzymes
  • FAD is required for the conversion of retinol to retinoic acid, which is essential for normal vision
  • FAD also plays a role in fatty acid oxidation

› Riboflavin is unstable in light and food sources of riboflavin should be stored in light-resistant containers. Dietary sources of riboflavin include the following (2,5,6,7,10,12,18):

  • Milk and milk products
  • Vitamin A-enriched breakfast cereals
  • Fatty fish, beef, and pork, including organ meats such as liver, kidney, and heart
  • Eggs
  • Dark green vegetables
  • Mushrooms

› Recommended daily intake of riboflavin (2,7,10,13,18)

  • Pediatric requirements
    – Adequate intake (AI) for infants < 6 months of age: 0.3 mg (based on 0.04 mg/kg)
    – AI for infants 6–12 months: 0.4 mg (based on 0.04 mg/kg)
    – Recommended dietary allowance (RDA) for children 1–3 years: 0.5 mg
    – RDA for children 4–8 years: 0.6 mg
    – RDA for children 9–13 years: 0.9 mg
    – RDA for females 14–19 years: 1 mg
    – RDA for males 14–19 years: 1.3 mg

  • Adult RDA
    – Women ≥ 19 years: 1.1 mg
    – Pregnant women > 19 years: 1.4 mg
    – Lactating women ≥ 19 years: 1.6 mg
    – Men ≥ 19 years: 1.3 mg
Riboflavin deficiency \( ^{2,10,11,12,18} \)

- Ariboflavinosis (i.e., riboflavin deficiency) is relatively rare in Western countries due to food and fortification programs. When ariboflavinosis occur, it is usually associated with malabsorption and accompanied by other nutrient deficiencies \( ^{2,5,7,10,18} \)
- The normal range for riboflavin level is 3–15 mcg/L. Patients with a value of < 2 mcg/L are considered to have riboflavin deficiency
- Risk factors for ariboflavinosis include \( ^{10} \)
  - alcoholism
  - anorexia nervosa or malnutrition
  - diabetes mellitus, cardiac or liver disease, or malignancy
  - chronic infections
  - taking the drug probenecid
  - being pregnant or lactating
  - infants
  - older adults
  - athletes
  - failure to consume adequate food sources of riboflavin; vegan vegetarians (i.e., following a diet with no dairy or meat) are at increased risk
- Signs and symptoms of ariboflavinosis include \( ^{10,18} \)
  - sore throat and glossitis
  - cheilosis (also called angular stomatitis), which is the development of cracks in the lips and the corners of the mouth
  - neuropathy, frequently on the feet
  - seborrheic dermatitis and other skin lesions
  - digestive disturbances
  - headache
  - depression
  - corneal vascularization, which can manifest as photophobia and itchy eyes \( ^{10} \)

Riboflavin Toxicity \( ^{2,10} \)

- Riboflavin toxicity is not a major concern because it is not stored in the body. Although taking large doses can cause the urine to become bright yellow because of the yellow color of riboflavin,

Risk of the interaction of riboflavin with medications \( ^{13} \)

- Probenecid can interfere with the absorption of riboflavin
- Riboflavin decreases the action of tetracycline

Recent research findings on riboflavin

- The effect of riboflavin on cardiovascular health has been of particular interest in research since riboflavin deficiency is associated with elevated blood levels of homocysteine, a putative cardiovascular disease (CVD) risk factor \( ^{2} \)
  - Scientists have identified polymorphism region near the gene that encodes methylenetetrahydrofolate reductase (MTHFR), the folate metabolizing enzyme, as one of 8 genomic loci linked to hypertension and CVD. Studies of this relationship have revealed that a significant gene-environment interaction exists, which increases the risk of hypertension and CVD. There is evidence that riboflavin could be the influencing environmental factor. Researchers suggest that improving riboflavin status via targeted riboflavin treatment in individuals with this genotype could prevent the development of hypertension in those individuals \( ^{8} \)
  - Results of a randomized controlled study analyzing the effect of riboflavin supplementation on the blood levels of homocysteine in 88 older adults found that oral supplementation at the rate of 10 mg/day significantly lowered homocysteine blood concentration in subjects with low riboflavin levels \( ^{14} \)
- Elevated blood levels of homocysteine have been associated with brain atrophy, which can lead to cognitive decline, dementia, and Alzheimer’s disease. Low vitamin B status has also been documented in persons with dementia and Alzheimer’s disease. While researchers have shown that vitamin B (including riboflavin) supplementation reduces homocysteine levels, study results have been conflicting on the efficacy of vitamin B supplementation for improving cognitive function \( ^{9,17} \)
• Riboflavin has been used for migraine prophylaxis based on findings of decreased levels of the vitamin in the blood and brain of patients with migraine and the idea that the pathology of migraine headaches might involve impaired mitochondrial oxygen metabolism in the brain. Authors of a systematic review of the effectiveness and safety of riboflavin supplementation for the prevention of migraine report that riboflavin is inexpensive, well tolerated, and effective for reducing the frequency of migraine headaches in adults.

• In a study investigating the effect of riboflavin supplementation on riboflavin levels in acutely ill older patients, researchers concluded that supplementation significantly improved riboflavin levels in the subjects, although the benefit diminished when supplementation ceased. Authors of another study reported that older patients with higher riboflavin intake had a lower risk of all-cause mortality.

• Scientists have studied the ability of lactic acid bacteria to synthesize riboflavin and have also developed genetically modified strains of lactic acid bacteria to enhance the biosynthesis of riboflavin. This fermentation-based approach is relevant in the production of functional foods that are riboflavin-enriched without the need for vitamin fortification. Lactic acid fermentation provides an environmentally friendly alternative to the traditional chemical synthesis of riboflavin and reduces the food production cost.

What We Can Do

› Become knowledgeable about the physiologic effects of riboflavin so you can accurately assess your patient’s characteristics and health education needs; share this information with your colleagues

› Assess your patients’ health and diet history and risk factors for ariboflavinosis

› Request that the treating clinician order riboflavin supplementation if beneficial to your patient

› Educate your patients about the importance of eating a balanced diet that includes good sources of riboflavin (e.g., milk, yogurt, and green, leafy vegetables)

› Educate your patients about all potential interactions between riboflavin-rich foods or supplements and any medications they may be receiving

› Assess your patients and their family members for knowledge deficits about the prescribed treatment regimen, and emphasize the importance of strict treatment regimen adherence and continued medical surveillance to monitor health status

Related Guidelines

› Patients with a serum riboflavin value of < 2 mcg/L are considered to have riboflavin deficiency. For guidelines on the recommended daily intake of riboflavin, see What We Know, above

References

1. Clark, R., Bennett, D., Parsh, S., Lewington, S., Skeaff, M., Eussen, S. J., ... Grodstein, F. (2014). Effects of homocysteine lowering with B vitamins on cognitive function and aging, concluded that lowering homocysteine via vitamin B supplementation had no effect on cognitive performance.


