

Folate

Physiological Functions

Folate (folacin or folic acid) participates as a coenzyme in reactions that require transfer of a single carbon moiety in different oxidative states as either a methenyl, methylene, or methyl group. These reactions typically involve synthesis of compounds such as thymidine, a pyrimidine base necessary for synthesis of DNA. In the absence of sufficient folic acid, uridine is substituted for thymidine resulting in hypomethylated DNA. These hypomethylated areas create fragile sites on chromosomes that exhibit vulnerability to breakage. In light of this, poor folate status has been linked to development of cancer. Increased intake of folate is also recommended for women of child-bearing age to prevent neural tube defects such as spinal bifida. Good periconceptional maternal folate status can reduce the risk of these defects in offspring by 50%.

Folate (with vitamin B12) is required for conversion of homocysteine to methionine. Elevated plasma homocysteine levels are a risk factor for atherosclerosis.

Factors Affecting Availability

Folate is highly sensitive to destruction by heat and light. Methods of cooking, processing or food storage can result in destruction of 50-95% of the folate content of food. Whole grains are excellent sources of folate, but almost all of the vitamin is destroyed in milling. Only about half of the folate consumed from food sources has acceptable bioavailability. Folate occurs naturally attached to multiple glutamic acid molecules which must be removed by hydrolysis prior to absorption by a vitamin B₁₂-dependent enzyme to form pteroylmonoglutamate. In general, foods with high proportions of the monoglutamate form have higher folate bioavailability irrespective of the total amount.

Because amounts of folate from natural dietary source are limited by extensive losses and low bioavailability, grain products are now fortified with folate on a mandatory basis. The synthetic form of folate in fortified foods is 1.7 times greater bioavailability than forms found naturally in food. Folate supplements also have 100% bioavailability.

Some medications can adversely affect folate status. These include oral contraceptives, antacids, aspirin, anticonvulsants, methotrexate, pyrimethamine, trimethoprim, trimetrexate and sulfasalazine.

Deficiency

Risk of folate deficiency is highest among women, elderly adults, smokers, and alcoholics. Alcohol not only decreases folate absorption, but also interferes with enterohepatic recycling which further increases the need for dietary folate. Smokers are also at risk of folate deficiency because cigarette smoke decreases folate activity in lung

tissue. Poor eating habits especially among the elderly can contribute to folate deficiency. Circumstances which promote rapid rates of cellular replication (e.g. burns and other tissue injury, pregnancy, prematurity, infection, and blood loss) also increase risk of folate deficiency. Folate deficiency is diagnosed from hematological parameters including red blood cell folate concentration and presence of megaloblastic red cells having normal hemoglobin concentration.

Toxicity

Evidence of toxicity associated with high folate intakes has not been reported. However, folate supplementation at high levels may interfere with the ability to detect presence of vitamin B12 deficiency because the expected megaloblastic changes will not occur. Untreated B₁₂ deficiency can result in irreversible neurological damage.

- ❖ *The upper limit of safety for folate established by the Food and Nutrition Board of the Institute of Medicine is 1000 µg daily for adults. Age-specific safety levels appear in the table below.*

Folate Tolerable Upper Intake Levels	
Life Stage	Folate (µg)
Infants	
0-6 mo	N/A
7-12 mo	N/A
Children	
1-3 y	300
4-8 y	400
Males, Females	
9-13 y	600
14-18 y	800
19-70 y	1000
70 y	1000
Pregnancy	
≤ 18 y	800
19-50 y	1000
Lactation	
≤ 18 y	800
19-50 y	1000

Requirements

The Daily Reference Intakes (DRI) for folate are shown in the table below.

Life Stage	Folate
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	(µg)
Infants	
0-6 mo	65
7-12 mo	80
Children	
1-3 y	150
4-8 y	200
Males	
9-13 y	300
14-18 y	400
19-30 y	400
31-50 y	400
51-70 y	400
70 y	400
Females	
9-13 y	300
14-18 y	400
19-30 y	400
31-50 y	400
51-70 y	400
70	400
Pregnancy	
18 y	600
19-30 y	600
31-50 y	600
Lactation	
18 y	500
19-30 y	500
31-50 y	500

Dietary Sources

Folate is obtained from green, leafy vegetables, liver, legumes, nuts, and some dairy foods. Fortified grain products are also an excellent source of high bioavailability folate. Although orange juice has a low total folate content, it is mostly in the more available monoglutamate form. See table for dietary sources of folate.

Folate Content of Food	
FOOD	Folate (µg)
Liver, chicken, 3.5 oz cooked	770
Liver, beef, 3.5 oz cooked	220
Blackeyed peas, boiled, 1 cup	210
Lentils, _ cup cooked	179
Beans, white, boiled, _ cup	144

Black eye peas, _ cup cooked	120
Broccoli, cooked, 1 cup	104
Spinach, cooked, _ cup	103
White pasta	98
Flour tortilla, 10"	88
Collard greens, ckd ,fresh _ cup	88
Romaine lettuce, 1 cup	76
Orange juice, 1 cup	75
Fresh spinach, 1 cup	58
Wheat germ, raw, 2 Tbl	50
Tofu, _ cup	55
Papaya cubes, 1 cup	53
Vegetable juice, 1 cup	51
Egg, yolk, 1	25
Banana, 1	22