

Folate: A Foundational B Vitamin

Key Topics: [Epigenetics](#)

March 13, 2021 • 2 min read

Folate is a water-soluble B vitamin, also known as vitamin B9. It is most well-known for its importance in early stages of pregnancy to prevent neural tube defects. However, this vitamin is critical for so much more – including disease prevention, DNA replication, and methylation balance.¹

Folate vs. Folic Acid vs. Methylfolate

Folic acid and folate are often used interchangeably, but the two are indeed structurally different. While folate is the natural reduced form found in food, folic acid is a synthetic, oxidized form found in fortified foods and lower-quality dietary supplements.² While folic acid is often regarded as more bioavailable, this form of B9 may not enter the cell as readily for utilization as other forms and is thought to bioaccumulate. This is most evident in people with specific single nucleotide polymorphisms (SNPs) that affect folate metabolism such as methyltetrahydrofolate reductase (MTHFR).^{3,4}

People with methylation SNPs may benefit from avoiding synthetic folic acid and supplementing with its active form, 5-methyl-tetrahydrofolate (5-MTHF). This is to prevent a possible build-up of unmetabolized folic acid, which is potentially genotoxic and may pose health risks, though studies have been mixed. While methylfolate supplements are commonly used in high doses, long term studies for the safety and efficacy of this practice are lacking.⁵ It is important to note that excessive folate levels can mask a vitamin B12 deficiency, which can cause irreversible damage.⁶

Many Functions of Folate

One of this vitamin's most important jobs involves methylation. Along with vitamin B12, riboflavin, choline, and other nutrients, folate facilitates the transfer of a one-carbon

methyl group (CH₃) from one molecule to another, which then activates or deactivates that molecule. Methylation plays an important role in:⁷

- Nutrient metabolism
- Hematopoiesis (red blood cell formation)
- Energy production
- DNA synthesis and repair
- Cell division
- Epigenetic regulation of gene expression
- Detoxification
- Neurotransmitter synthesis
- Neural tube formation and central nervous system (CNS) development
- Healthy mean corpuscular volume (MCV), as low levels can cause red blood cells to become too large (megaloblastic anemia)⁸

Through these various processes, this vitamin is protective of health with regard to many different areas, including cardiovascular health, cancer prevention, and healthy aging.⁹

Cancer Prevention

Folate is instrumental in DNA synthesis and repair, cell division, and methylation balance. Alterations in these processes are identified in the etiology of developing cancer. In fact, poor folate status may be linked to colon, lung, esophageal, adenocarcinoma, and gastroenterological cancers.¹⁰

Cardiovascular Health

Together with vitamin B₁₂, folate facilitates the metabolism of homocysteine to methionine. Methionine is a sulfur-containing amino acid and methyl donor, which is a building block of glutathione. Homocysteine is an amino acid, which, if not metabolized, can contribute to vascular damage and blood clots. High levels of homocysteine are associated with cardiovascular disease.^{11,12}

Cognitive Health and Neurotransmitter Function

In addition to being instrumental in neural tube and CNS development in the fetus, folate may also have a role in cognitive health throughout the lifecycle. Like cardiovascular risk, high homocysteine levels related to folate insufficiency are also associated with cognitive decline and dementia; deficiency among seniors may accelerate the brain's aging process.¹³ Folate and folic acid supplementation have been found to improve both cognition and levels of inflammation in people with Alzheimer's disease, who were found to also have low folate levels.¹⁴

Sources of Natural Folate

Named after the Italian word for foliage, *folato*, folate is the natural form of the vitamin found in many foods, including – as the name would suggest – dark green leafy vegetables. The following foods are rich sources of folate:¹⁵

- Dark leafy greens and cruciferous vegetables: spinach, asparagus, broccoli, Brussels sprouts, kale, bok choy, escarole, collard greens, beet greens, mustard greens, and turnip greens
- Beans and Legumes: lentils, black eyed peas, pinto beans, garbanzo beans, navy beans, black beans, and kidney beans
- Animal Sources: beef liver

With such critical roles through the body and across systems, it is no wonder that vitamin B9, also known as folate, is considered a foundational vitamin.