

Vitamin B9 - description, benefits, effects on the body and best sources

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Folic acid is a water-soluble B vitamin. It is also known as **folate** and vitamin **B-9**. Plays an important role in the process of cell division and creation in some organs and bone marrow. A key function of folic acid is also to help form the spinal cord and nervous system of the fetus in the womb. Like other B vitamins, folic acid promotes energy production in the body.

In our body, coenzymes of vitamin B9 (folate) interact with one-carbon units in a variety of reactions that are vital for the metabolism of nucleic and amino acids. Folate is needed to maintain the vital activity of all cells.

The terms folate, folic acid, and vitamin B9 are often used interchangeably. While folate is present in both food and the human body in a metabolically active form, folic acid is often consumed in vitamin supplements and fortified foods.

Keywords: vitamin B9, vitamin B9, benefits, harms, beneficial properties, contraindications

Other names: folic acid, folacin, folate, pteroylglutamic acid, vitamin B9, vitamin Bc, vitamin M.

Chemical formula: C 19 H 19 N 7 O 6

Foods with the highest folic acid content [6]

Product	Content, Dietary Folate Equivalent per 100g
Turkey liver	677
Chickpeas, raw	557
Edamame beans, frozen	303
beef liver	290
Wheat germ	281
Peanut	240
Sunflower seeds	237
Spinach, fresh	194

turnip tops	194
Lentils, cooked	181
Asparagus, cooked	149
Romaine lettuce	136
Pinto beans	118
Beets, raw	109
Walnut	98
Rucola	97
Flaxseeds	87
Avocado	81
Broccoli	63
curly cabbage	62
Brussels sprouts	61
Cauliflower	57
Red beans, cooked	47
Chicken egg	47
Almond	44
White cabbage	43
Mango	43
Corn	42
Papaya	37
Celery	36
Orange	thirty
Kiwi	25
Strawberry	24
Raspberry	21
Banana	twenty
Carrot	19
honey melon	19
Kohlrabi	16
Tomato	fifteen
Potato	fifteen
Grapefruit	13
Lemon	eleven
Bell pepper	ten

See also Top 100 Natural Sources of Vitamin B9.

Daily requirement for vitamin B9

In order to establish the daily intake of vitamin B9, the so-called " *dietary folate equivalent* " (in English - DFE) was introduced. The reason for this was the better absorption of synthetic folic acid, compared with natural folate obtained from food. PFE is calculated as follows:

- 1 microgram of food folate equals 1 microgram of PFE
- 1 microgram of folic acid taken with food or from foods fortified with it equals 1.7 micrograms of PFE

• 1 microgram of folic acid (a synthetic dietary supplement) taken on an empty stomach equals 2 micrograms of PFE.

For example: from a meal containing 60 micrograms of natural folate, the body receives 60 micrograms of a Dietary Equivalent. From a serving of pasta fortified with 60 micrograms of synthetic folic acid, we get 60 * 1.7 = 102 micrograms of a Food Equivalent. And one 400 mcg folic acid tablet will give us 800 mcg of a Dietary Equivalent.

In 2015, the European Scientific Committee on Nutrition established the following daily intake of vitamin B9:

Age	Recommended Amount Men (mcg Dietary Folate Equivalent/day)	
7-11 months	80 mcg	80 mcg
1-3 years	120 mcg	120 mcg
4-6 years old	140 mcg	140 mcg
7-10 years old	200 mcg	200 mcg
11-14 years old	270 mcg	270 mcg
15 years and older	330 mcg	330 mcg
Pregnancy		600 mcg
lactating		500 mcg

Due to the fact that vitamin B9 plays a very important role in pregnancy, the daily requirement for pregnant women is many times higher than the usual daily requirement. However, the formation of the neural tube of the embryo often occurs before a woman knows she is pregnant, and it is at this point that folic acid can play a critical role. For this reason, some experts recommend regularly taking courses of vitamins, which include 400 micrograms of folic acid. It is believed that even when taking such a dose and eating foods containing folate, it is almost impossible to exceed the maximum safe amount of vitamin B9 per day - 1000 mcg [1].

Increasing the body's need for vitamin B9

Generally, serious B9 deficiency in the body is rare, however, some populations may be at risk of deficiency. These groups are:

- **people with alcohol dependence**: alcohol disrupts the metabolism of folate in the body and accelerates its breakdown. In addition, people suffering from alcoholism are often malnourished and do not get enough vitamin B9 from food.
- Women of childbearing age: Women of childbearing potential should take enough folic acid to avoid developing a neural tube defect in the early stages of pregnancy.
- **pregnant women**: during pregnancy, vitamin B9 plays an important role in nucleic acid synthesis.
- **people with poor digestibility of food**: diseases such as dengue fever, celiac disease and irritable bowel syndrome, gastritis can interfere with the absorption of folate ^[6].

Chemical and physical properties

Folic acid is a yellow crystalline substance, slightly soluble in water, but insoluble in fatty solvents. Resistant to heat only in alkaline or neutral solutions. Destroys under the influence of sunlight. Almost or completely odorless [7].

Structure and forms

Dietary folate exists predominantly in the polyglutamyl form (containing a few glutamate residues), while folic acid, the synthetic vitamin form, is a monoglutamate containing only one glutamate moiety. In addition, natural folates are molecules with a reduced molecular weight, while folic acid is completely oxidized. These chemical differences have significant implications for vitamin bioavailability, with folate being significantly more bioavailable than naturally occurring dietary folate at equivalent intake levels [8].

The folic acid molecule consists of 3 units: glutamic acid, p-aminobenzoic acid and pterin. The molecular formula is C ₁₉ H ₁₉ N ₇ O ₆. The various B9 vitamins differ from each other in the number of glutamic acid groups present. For example, folic acid contains one Lactobacillus casei fermentation factor three and Bc conjugate-7 glutamic acid groups. Conjugates (i.e., compounds having more than one glutamic acid group in the molecule) are not effective in some species because these species do not have the enzyme needed to release the free vitamin ^[7].

Useful properties and effects on the body

The benefits of vitamin B9 for the body:

- affects the course of a healthy pregnancy and the proper development of the fetus: folic acid prevents the development of defects in the nervous system of the fetus, underweight, premature birth, and this occurs in the very early stages of pregnancy.
- antidepressant: folic acid is believed to help manage depression and improve emotional well-being.
- helps in protein metabolism.
- Acne Treatment: Vitamin B9 is considered a powerful antioxidant that helps detoxify the body and improve skin condition.
- maintaining heart health: folic acid intake reduces blood levels of homocysteine, an increased amount of which can lead to the risk of cardiovascular disease. In addition, the vitamin B complex, which includes folic acid, reduces the risk of stroke.
- Reducing the risk of cancer: there is evidence that insufficient folic acid intake is associated with the development of breast cancer in women.

Folic acid metabolism in the body

Folate functions as a coenzyme in nucleic acid synthesis and amino acid metabolism. Once ingested, dietary folates are hydrolyzed to the monoglutamate form in the intestine before they are absorbed through the mucosa by active transport substances. Before entering the bloodstream, the monoglutamate form is reduced to tetrahydrofolate (THF) and converted to the methyl or formyl form [1]. The main form of folate in plasma is 5-methyl-THF. Folic acid can also be detected in the blood unchanged (unmetabolized folic acid), but it is not known whether this form has any biological activity [8]

In order for folate and its coenzymes to cross cell membranes, special transporters are required. They include the reduced folate transporter (RFC), the proton-coupled folate transporter (PCFT), and the folate receptor proteins, $FR\alpha$ and $FR\beta$. Folate homeostasis is maintained by the ubiquity of folate transporters, although their number and importance varies in different body tissues. PCFT plays an

important role in folate transplantation because mutations affecting the gene encoding PCFT cause hereditary folate malabsorption. Defective PCFT also leads to impaired folate transport to the brain. FR α and RFC are also critical for folate transport across the barrier between the circulatory system and the central nervous system. Folate is essential for the proper development of the embryo and fetus. It is known that the placenta is responsible for the entry of folate into the fetus, resulting in higher folate concentrations in the baby than in the mother. All three receptor types are associated with transport of folate across the placenta during pregnancy [6].

Interaction with other trace elements

Folate and vitamin B12 together form one of the most powerful micronutrient pairings. Their interaction supports some of the most fundamental processes of cell division and replication. In addition, they together participate in the metabolism of homocysteine. Although these two vitamins can be obtained naturally from two completely different types of foods (vitamin B12 from animal products: meat, liver, eggs, milk, and vitamin B9 from leafy vegetables, beans), their relationship is very important to the body. They act as cofactors in the synthesis of methionine from homocysteine. If synthesis does not occur, then the level of homocysteine may be elevated, which is often associated with the risk of developing cardiovascular diseases and stroke ^[9].

An important metabolic interaction in vitamin B9 occurs with riboflavin (vitamin B2). The latter is the precursor of a coenzyme involved in folate metabolism. It converts folate to its active form, 5-methyltetrahydrofolate.

Vitamin C may limit the degradation of natural folate coenzymes and supplemental folic acid in the stomach and thus improve folate bioavailability [8].

The most useful food combinations with vitamin B9

Vitamin B9 is useful to combine with other B vitamins.

For example, in a salad with kale, sunflower seeds, feta, barley, red onion, chickpeas, avocado and lemon dressing. Such a salad will provide the body with vitamins B3, B6, B7, B2, B12, B5, B9.

A great recipe for breakfast or a light lunch is a sandwich made from whole grain bread, smoked salmon, asparagus and poached eggs. This dish contains vitamins such as B3 and B12, B2, B1 and B9.

Food is the best source of vitamins. Therefore, the possibility of taking vitamins in the form of medicines should be considered if there are appropriate indications. There is evidence that vitamin preparations, if used incorrectly, not only do not benefit, but can also harm the body.

Application in official medicine

Pregnancy

Folic acid is used in medicine for many reasons. First of all, it is prescribed to pregnant women and those who are preparing for conception. The growth and development of the fetus is characterized by active cell division. Adequate folate levels are critical for DNA and RNA synthesis. Due to a lack of folic acid, between the 21st and 27th days after conception, a disease called *neural tube defect can develop*. As a rule, during this period, the woman does not yet know that she is pregnant, and cannot take appropriate measures by increasing the amount of folate in the diet. This disease leads to a number of undesirable consequences for the fetus - brain damage, encephalocele, spinal lesions.

Congenital heart anomalies are the leading cause of childhood death and can also lead to death in adulthood. According to the European Registry of Congenital Anomalies and Twins, consumption of at least 400 micrograms of folic acid per day one month before conception and for 8 weeks after conception reduced the risk of congenital heart defects by 18 percent.

Maternal folate levels may affect the risk of congenital cleft palate anomalies. A study in Norway showed that taking vitamin supplements with at least 400 micrograms of folic acid reduced the risk of cleft palate by 64%.

Low birth weight is associated with an increased risk of mortality during the first year of life and may also affect health status in adulthood. A recent systematic review and meta-analysis of eight controlled studies found a positive association between folic acid intake and birth weight.

Elevated blood levels of homocysteine have also been associated with increased rates of miscarriage and other pregnancy complications, including preeclampsia and placental abruption. A large retrospective study showed that plasma homocysteine levels in women directly affected the presence of adverse pregnancy outcomes and complications, including preeclampsia, preterm birth, and very low birth weight. The regulation of homocysteine, in turn, occurs with the participation of folic acid.

Thus, it is wise to take folic acid, under medical supervision, throughout pregnancy, even after neural tube closure, to reduce the risk of other problems during pregnancy. Moreover, recent studies have found no evidence of an association between folate intake during pregnancy and adverse health outcomes in children, such as asthma and allergies.

Cardiovascular diseases

More than 80 studies show that even moderately elevated blood levels of homocysteine increase the risk of cardiovascular disease. The mechanism by which homocysteine may increase the risk of developing vascular disease is still the subject of much research, but may include adverse effects of homocysteine on blood clotting, arterial vasodilation, and arterial wall thickening. Folate-rich diets have been associated with a reduced risk of cardiovascular disease, including coronary heart disease, myocardial infarction (heart attack), and stroke. A 10-year study of 1,980 men in Finland found that those who consumed the highest amount of dietary folate had a 55% lower risk of sudden heart disease compared to those who consumed the least amount of folate. Of the three B vitamins that regulate homocysteine levels, folic acid has been shown to have the greatest effect on lowering basal levels, provided there is no concomitant vitamin B12 or vitamin B6 deficiency. Increasing folate intake through folate-rich foods or supplements has been found to decrease homocysteine levels.

Despite controversy regarding the role of lowering homocysteine in the prevention of cardiovascular disease, some studies have examined the effect of folic acid supplementation on the development of atherosclerosis, a known risk factor for vascular disease. Although recent trials have not shown that folic acid directly protects the heart, low folate intake is a known risk factor for cardiovascular disease.

Cancer diseases

Cancer is thought to be caused by damage to the DNA, either from excessive DNA repair processes or from mis-expression of key genes. Due to the important role of folate in DNA and RNA synthesis, it is possible that insufficient vitamin B9 intake contributes to genomic instability and chromosomal defects that are often associated with cancer development. In particular, DNA replication and repair are critical for maintaining the genome, and nucleotide shortages caused by folate deficiency can lead to genomic instability and DNA mutations. Folate also controls the cycle of homocysteine/methionine and S-adenosylmethionine, a methyl donor for methylation reactions. Thus, folate deficiency can

impair DNA and protein methylation and alter the expression of genes involved in DNA repair, cell division, and cell death. Global DNA hypomethylation, a typical hallmark of cancer, causes genomic instability and chromosomal fractures.

Eating at least five servings of fruits and vegetables a day is currently associated with a reduced incidence of cancer. Fruits and vegetables are excellent sources of folic acid, which may play a role in their anti-carcinogenic effect.

• Alzheimer's disease and dementia

Alzheimer's disease is the most common form of dementia. One study found an association between increased intake of folate-rich fruits and vegetables and a reduced risk of dementia in women.

Through its role in nucleic acid synthesis and providing enough methyl for methylation reactions, folate affects normal brain development and function not only during pregnancy and after birth, but also later in life. In one cross-sectional study of older women, patients with Alzheimer's disease had significantly higher homocysteine levels and lower blood folic acid concentrations than healthy individuals. In addition, the scientists concluded that the prevention of dementia is influenced by long-term blood levels of folate, and not recent folate use. A two-year, randomized, placebo-controlled trial in 168 elderly patients with mild cognitive impairment found benefits from daily intake of 800 mcg folic acid, 500 mcg vitamin B12, and 20 mg vitamin B6. Atrophy of certain areas of the brain affected by Alzheimer's disease was observed in individuals of both groups, and this atrophy correlated with cognitive decline; however, the group treated with B vitamins experienced less gray matter loss compared to the placebo group (0.5% vs. 3.7%). The most beneficial effect was found in patients with higher baseline homocysteine concentrations, suggesting the importance of lowering circulating homocysteine in the prevention of cognitive decline and dementia. Although encouraging, B-vitamin supplementation needs to be further explored in larger studies that evaluate long-term outcomes such as the incidence of Alzheimer's disease [8].

Depression

Low folate levels are associated with depression and poor response to antidepressants. In a recent study of 2,988 people aged 1 to 39 years in the United States, serum and red blood cell folic acid concentrations were significantly lower in those with severe depression than in those who had never been depressed. A study of 52 men and women diagnosed with a depressive disorder showed that only 1 of 14 patients with low folate levels responded to antidepressant treatment, compared with 17 of 38 patients with normal folate levels.

Although folic acid supplementation has not been suggested as a replacement for conventional antidepressant therapy, it may be useful as an adjunct. In a UK study, 127 depressed patients were chosen to take either 500 micrograms of folic acid or a placebo in addition to 20 mg of fluoxetine (an antidepressant) daily for 10 weeks. Although the effects in men were not statistically significant, women who received fluoxetine plus folic acid fared much better than those who received fluoxetine plus placebo. The authors of the study concluded that folate "may have a potential role as an adjunct to mainstream depression treatment" [6] .

Dosage forms of vitamin B9

The most common dosage form of folic acid is tablets. The dosage of the vitamin may be different, depending on the purpose of the drug. In prenatal vitamins, the most common dosage is 400 mcg, since this amount is considered sufficient for the healthy development of the fetus. Often, folic acid is

included in vitamin complexes, along with other B vitamins. Such complexes can be in the form of tablets, as well as in the form of chewable plates, soluble tablets, and injections.

To lower the level of homocysteine in the blood, 200 mcg to 15 mg of folic acid per day is usually prescribed. In the treatment of depression, take 200 to 500 mcg of the vitamin per day, in addition to the main treatment. Any dosage must be prescribed by the attending physician [10].

Folic acid in folk medicine

Traditional healers, as well as doctors in traditional medicine, recognize the importance of folic acid for women, especially pregnant women, as well as its role in preventing heart disease and anemia.

Folic acid is found, for example, in strawberries. Its fruits are recommended for diseases of the kidneys, liver, blood vessels and heart. In addition to folate, strawberries are also rich in tannins, potassium, iron, phosphorus, and cobalt. For medicinal purposes, fruits, leaves and roots are used [11].

Folate, along with essential oils, vitamin C, carotene, flavonoids, and tocopherol, is found in parsley seeds. The plant itself has a bile and diuretic effect, relieves spasms and cleanses the body. Infusion and decoction of seeds helps with swelling, inflammation of the mucous membrane of the urinary tract. In addition, parsley infusion is prescribed for uterine bleeding [12].

Grapes are considered a rich source of folic acid in folk medicine. They contain from 65 to 85 percent of water, from 10 to 33 percent of sugar, and a large number of useful substances - various acids, tannins, potassium, magnesium, calcium, manganese, cobalt, iron, vitamins B1, B2, B6, B9, A, C, K, P, PP, enzymes [13].

Latest Scientific Research on Vitamin B9

- The use of high doses of folic acid does not affect the risk of developing preeclampsia. It is a serious illness characterized by the development of abnormally high blood pressure during pregnancy and other complications. This condition is dangerous for both mother and child. It has previously been suggested that high doses of folate may reduce the risk of developing it in women who are predisposed to the disease. These include those who have high blood pressure chronically; women with diabetes or obesity; pregnant with twins; as well as those who have had preeclampsia in previous pregnancies. The study involved more than 2 thousand women pregnant for a period of 8 to 16 weeks. It was found that taking 4 mg of folic acid daily did not affect the risk of developing the disease compared with those who took placebo in addition to the standard 1 mg of folate (14.8% of cases and 13.5% of cases, respectively). However, physicians still recommend taking a low dose of folic acid before and during pregnancy to prevent the development of congenital diseases [15].
- Irish scientists have determined that a significant number of people over the age of 50 are deficient in vitamin B12 (1 in 8 people) and folic acid (1 in 7 people). The degree of deficiency varies depending on lifestyle, health status and nutrition. Both vitamins are essential for the health of the nervous system, brain, red blood cell production, and DNA division. It has also been found that the percentage of folic acid deficiency increases with age from 14% among 50-60 year olds to 23% in those over 80 years of age. It was most common in smokers, obese people, and those who lived alone. Vitamin B12 deficiency was more common in those who smoke (14%), live alone (14.3%) and people from low socioeconomic backgrounds [16].
- British scientists insist on the general enrichment of flour and other products with folic acid. According to the authors of the study, every day in Britain, on average, two women are forced to terminate a pregnancy due to a neural tube defect, and every week two children are born affected by this disease. Britain is one of the countries where food fortification with folic acid

is not the norm, unlike the US and other countries. "If the UK had legalized folate fortification in 1998, as it did in America, about 3,000 birth defects could have been avoided by 2007," states Professor Joan Morris [14].

Use in cosmetology

Folic acid plays a very important role in maintaining the natural beauty of the skin. It contains a concentration of antioxidants that reduce the activity of oxidative processes and neutralize free radicals present in the environment. The skin-care properties of folic acid also help maintain skin hydration by strengthening the skin barrier. This retains moisture and reduces dryness.

In cosmetics, folic acid products are most commonly included in moisturizing lotions and creams, which when applied topically can help improve overall skin quality and appearance.

Use in animal husbandry

Folic acid deficiency has been experimentally detected in many animal species, manifesting itself as anemia with a decrease in the number of leukocytes. Tissues with a high rate of cell growth or tissue regeneration are mainly affected, such as the epithelial lining of the gastrointestinal tract, the epidermis, and the bone marrow. In dogs and cats, anemia is most commonly associated with folic acid deficiency caused by intestinal malabsorption syndromes, malnutrition, folic acid antagonists, or increased folic acid requirements due to blood loss or hemolysis. For some animals, such as chickens, guinea pigs, monkeys and pigs, having enough folic acid in the diet is essential. In other animals, including dogs, cats, and rats, folic acid produced by the gut microflora is usually sufficient to meet requirements. Therefore, signs of deficiency may develop if an intestinal antiseptic is also included in the diet to inhibit bacterial growth. Folic acid deficiency occurs in dogs and cats usually only when antibiotics are taken. It is likely that most of the daily requirement for folic acid is met by bacterial synthesis in the gut.

Contraindications and warnings

About 50-95% of folic acid is destroyed during cooking and preservation. Exposure to sunlight and air is also detrimental to folate. Foods high in folic acid should be stored in a dark vacuum container at room temperature [18].

Signs of a folic acid deficiency

Deficiency of folic acid alone is rare, usually associated with other nutrient deficiencies due to malnutrition, alcoholism, or absorption disorders. Symptoms typically include weakness, trouble concentrating, irritability, heart palpitations, and shortness of breath. In addition, there may be pain and ulcers on the tongue; problems with skin, hair, nails; problems in the gastrointestinal tract; elevated levels of homocysteine in the blood ^[6].

Signs of excess vitamin B9

As a rule, excessive consumption of folic acid does not carry side effects. In rare cases, very high doses of folate can harm the kidneys and cause loss of appetite. Taking large amounts of vitamin B9 can mask a vitamin B12 deficiency. The established maximum daily intake of folate for an adult is 1 mg $^{[1]}$.

Some medicines affect the absorption of vitamin B9 in the body, among them:

- oral contraceptives;
- methotrexate (used in the treatment of cancer and autoimmune diseases);
- antiepileptic drugs (phenytoin, carbamazepine, valproate);
- sulfasalazine (used to treat ulcerative colitis) [6].

Discovery history

Folate and its biochemical role were first discovered by British researcher Lucy Wills in 1931. In the second half of the 1920s, active research was carried out on the nature of pernicious anemia and methods of its treatment - thus vitamin B12 was discovered. Dr. Wills, however, decided to focus on the narrower subject of anemia in pregnant women. She was criticized for such a narrow approach, but the doctor did not stop trying to find the cause of the severe anemia that pregnant women in the British colonies suffered from. Studies on rats did not bring the desired results, so Dr. Wills decided to conduct an experiment on primates.

After trying many substances, and rejecting all possible hypotheses by elimination, in the end, the researcher decided to try using cheap brewer's yeast. And finally got the desired effect! She determined that the nutrient found in yeast is essential to prevent anemia during pregnancy. Some time later, Dr. Wills included in her study attempts to use various substances by pregnant women, and brewer's yeast again gave the desired result. In 1941, folic acid derived from spinach was named and isolated for the first time. That is why the name folate comes from the Latin folium - leaf. And in 1943, the vitamin was obtained in pure crystalline form.

Since 1978, folic acid has been used in combination with the anticancer drug 5-fluorouracil. First synthesized in 1957 by Dr. Charles Heidelberger, 5-FU has become an effective drug against certain types of cancer, but has had severe side effects. Two students of the doctor discovered that folic acid can significantly reduce them, while at the same time increasing the effectiveness of the drug itself.

In the 1960s, scientists began to investigate the role of folic acid in preventing neural tube defects in the embryo. It was found that vitamin B9 deficiency can have very serious consequences for the child, and also that usually a woman does not get enough of the substance from food. Therefore, in many countries it was decided to enrich foods with folic acid. In America, for example, folate is added to many grain products - bread, flour, cornstarch, pasta and noodles - as they are staple foods for most of the population. Thanks to this, the number of cases of neural tube defects has been reduced by 15-50% in the United States. [2-4].

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Abstract. The article discusses the main properties of vitamin B9 and its effect on the human body. A systematic review of modern specialized literature and relevant scientific data was carried out. The best natural sources of vitamin B9 are indicated. The use of vitamin a in various types of medicine and the effectiveness of its use in various diseases are considered. The potentially adverse effects of vitamin B9 on the human body under certain medical conditions and diseases are analyzed separately.