



Drugs and Supplements

Folate

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Background

Folate and folic acid are forms of a water-soluble B vitamin. Folate occurs naturally in food, and folic acid is the synthetic form of this vitamin. Folic acid is well-tolerated in amounts found in fortified foods and supplements. Sources include cereals, baked goods, leafy vegetables (spinach, broccoli, lettuce), okra, asparagus, fruits (bananas, melons, lemons), legumes, yeast, mushrooms, organ meat (beef liver, kidney), orange juice, and tomato juice. Folic acid is frequently used in combination with other B vitamins in vitamin B complex formulations.

Folic acid supplements are effective for increasing folate levels in blood and decreasing symptoms associated with low folate levels. Folic acid supplementation, with and without other B vitamins, reduce levels of homocysteine in blood (a cardiovascular risk factor).

Folic acid supplements are suggested for use in women of childbearing age in order to prevent neural tube defects. Neural tube defect risk appears to have decreased in many countries since folic acid fortification of flour and cereals.

Folic acid is also of interest with respect to cognitive enhancement, cancer, psychiatric illnesses, and cardiovascular conditions, although conclusions may not be drawn for many of these uses at this time. Some concern exists with respect to increased folic acid intake masking symptoms of vitamin B12 deficiency, especially in the elderly population.

Dosing

The below doses are based on scientific research, publications, traditional use, or expert opinion. Many herbs and supplements have not been thoroughly tested, and safety and effectiveness may not be proven. Brands

may be made differently, with variable ingredients, even within the same brand. The below doses may not apply to all products. You should read product labels, and discuss doses with a qualified healthcare provider before starting therapy.

Adults (over 18 years old)

General: The daily suggested intake levels of folic acid are as follows: males over 13 years, 400 micrograms; females over 13 years, 400-600 micrograms; pregnancy all ages, 400-600 micrograms; breastfeeding females of all ages, 500 micrograms. The maximum daily intake level of folic acid for people 19 years and older (including pregnant or breastfeeding women), 1,000 micrograms.

For anemia caused by folate deficiency, 1-5 milligrams has been taken by mouth daily until recovery.

For antiseizure drug-induced folate deficiency, 15 milligrams has been taken by mouth daily under the supervision of a qualified healthcare provider.

For bipolar disorder, 200 international units of folic acid has been taken by mouth daily for 52 weeks in patients stabilized on lithium. Three milligrams of folic acid have been taken by mouth daily for three weeks in patients starting valproic acid therapy.

For cancer (general), 0.2-40 milligrams of folate or folic acid (either taken alone or in combination with aspirin, vitamin B6, or vitamin B12) has been taken by mouth daily for 3-8 years, with mixed results.

For cognitive effects, 0.75-15 milligrams of folic acid has been taken by mouth daily for 1-36 months.

For colorectal cancer, 0.5-5 milligrams of folic acid has been taken by mouth daily for 3-8 years with mixed results.

For chronic kidney disease, 2-15 milligrams of folic acid has been taken by mouth daily, every other day or three times weekly, for a follow-up duration of 1-3.6 years.

For depression, 0.5-3 milligrams or 200 international units of folic acid or 15-50 milligrams of methylenetetrahydrofolate have been taken by mouth daily for 3-52 weeks.

For diabetes, 5 milligrams of folic acid has been taken by mouth daily for 1-6 months.

For folate deficiency, 250-1,000 micrograms has been taken by mouth daily. In addition, for severe folate deficiency, 1-5 milligrams has been taken by mouth daily until blood levels are corrected and documented by a qualified healthcare professional.

For fragile X syndrome, 10-250 milligrams of folic acid has been taken by mouth daily for 2-8 months with a lack of effect on symptoms.

For heart disease, 0.8-40 milligrams of folic acid have been taken by mouth daily for 3-88 months.

For high homocysteine levels, 0.2-5 milligrams of folic acid has been taken by mouth for 21-168 days.

For high blood pressure, 5-10 milligrams of folic acid has been taken by mouth for 2-16 weeks.

For methotrexate toxicity, 1-27.5 milligrams of folic acid or 1-20 milligrams of folinic acid has been taken by mouth daily or weekly for up to 12 weeks.

For the prevention of birth defects, wheat flour fortified with folic acid has been taken by mouth before pregnancy and during the first two months of pregnancy. Doses of 0.36-5 milligrams have been taken by mouth daily.

For the prevention of pregnancy complications (other), 0.25-5 milligrams of folic acid have been taken by mouth daily for 12-24 weeks.

For stroke, 0.5-40 milligrams of folic acid have been taken by mouth daily for 6-88 months.

For vein clots, 5 milligrams of folic acid has been taken by mouth once daily during pregnancy.

For vitiligo, 5 milligrams has been taken by mouth twice daily.

For gum overgrowth caused by phenytoin, folic acid has been applied to the gum.

For pregnancy-related gum disease, folic acid has been applied to the gum.

Children (under 18 years old)

The daily suggested intake levels of folic acid are as follows: babies 0-6 months, 65 micrograms; 7 to 12 months, 80 micrograms; children 1-3 years, 150 micrograms; 4-8 years, 200 micrograms; males 9-13 years, 300 micrograms; males over 13 years, 400 micrograms; and females 9-13 years, 300 micrograms.

The maximum daily intakes are as follows: for children 1-3 years-old, 300 micrograms; for children 4-8 years-old, 400 micrograms; for children 9-13 years-old, 600 micrograms; and for adolescents 14-18 years-old, 800 micrograms. Folic acid injection contains benzyl alcohol (1.5 percent), and extreme care should be used when given to newborns. Folic acid injections should be given by a healthcare provider.

For fragile X syndrome, 10-250 milligrams has been taken by mouth daily for 2-8 months with a lack of effect on symptoms.

For general health maintenance, 0.005-15 milligrams has been taken by mouth daily for two weeks to 18 months, with mixed results.

Evidence

These uses have been tested in humans or animals. Safety and effectiveness have not always been

proven. Some of these conditions are potentially serious, and should be evaluated by a qualified healthcare provider.

Key to grades

- A** Strong scientific evidence for this use
- B** Good scientific evidence for this use
- C** Unclear scientific evidence for this use
- D** Fair scientific evidence against this use (it may not work)
- F** Strong scientific evidence against this use (it likely does not work)

Grading rationale

A

Anemia (caused by folate deficiency)

Folate deficiency may cause megaloblastic anemia, a blood disorder in which there are very large red blood cells. If the cause is folate deficiency, then treatment with folate is the standard approach. People with anemia should see a medical professional to identify the underlying cause.

A

Folate deficiency

Folate deficiency will occur if the body does not get enough folic acid from dietary intake. Folic acid is effective in the treatment of some complications of folate deficiency.

A

Folate deficiency in alcoholics

Folate deficiency has been seen in alcoholics. Alcohol affects the body's ability to absorb folate and also increases folate in the urine. Many alcohol abusers have poor quality diets that do not provide the suggested intake of folate. Increasing folate intake through diet, or folic acid intake through fortified foods or supplements, may benefit the health of alcoholics.

Heart disease (high homocysteine levels)

A

High blood levels of the amino acid homocysteine is considered a significant risk factor for heart disease. B vitamins, including folate, affect homocysteine levels.

A

Prevention of pregnancy complications (birth defects)

Consuming a high level of folate and taking folic acid supplements by mouth during pregnancy helps reduce the risk of birth defects in the infant.

B

Methotrexate toxicity

Folate may help people being treated with long-term, low-dose methotrexate for rheumatoid arthritis (RA) or psoriasis. Folate deficiency may cause side effects including stomach problems and inflammation, hair loss, anemia, and high homocysteine levels, which are linked to heart disease. People who have experienced side effects may need to continue taking folic acid for the duration of methotrexate therapy. People receiving methotrexate for cancer should avoid folic acid supplements, unless suggested by their doctor. There is some evidence that folic acid supplements reduce the effectiveness of methotrexate in the treatment of some cancers.

C

Acute lymphocytic leukemia (cancer of the white blood cells)

Early evidence suggests that vitamin use during pregnancy might protect against acute lymphoblastic leukemia. The effects of folate alone are not clear. High-quality research on folate supplementation is needed before a conclusion may be made.

C

Amenorrhea (lack of menstrual period)

Early studies show that folic acid treatment may improve health, including levels of homocysteine, in women with absent menstrual periods caused by exercise. Further study is needed.

C

Anemia (blood disorder caused by iron deficiency)

The effect of folic acid on iron-deficiency anemia is not clear. More research is needed in this area before a firm conclusion can be made.

C

Arsenic poisoning

Folate may lower blood levels of arsenic and may help prevent illnesses caused by arsenic. Additional research is needed in this area.

C

Bipolar disorder

Folic acid deficiency has been found among people with depression and has been linked to poor response to treatment. Higher blood levels of homocysteine are linked to increased depression in later life. Folate has been used for enhancing treatment response to antidepressants. Further study is needed to determine the effects on bipolar people.

C

Cancer (general)

Early evidence on the use of folate seems promising for decreasing the risk of breast, cervical, pancreatic, and stomach cancer. However, currently there is a lack of strong evidence available to support this use of folate.

C

Chronic fatigue syndrome

Some people with chronic fatigue syndrome (CFS) also have decreased folic acid levels. Daily injections of a combination of folic acid, bovine liver extract, and vitamin B12 for three weeks lacked benefit in early research. Further study is needed in this area.

C

Cognitive function

Combined B vitamin supplementation lacked benefit in early research on cognitive decline in women with heart disease or heart disease risk factors. The link between low folate levels and cognitive impairment in older people is unclear. The effect of folic acid in combination with multivitamins on children's cognitive function has also been studied. Further research is needed in this area.

C

Coronary artery disease

Folic acid may benefit coronary artery disease in terms of blood pressure control. More research is needed in this area. People with this condition need to be treated by a qualified healthcare provider.

C

Dementia

Dementia and Alzheimer's disease have been linked to low folate levels and high homocysteine levels. B vitamins, including folate, and the prevention of dementia are currently being studied. However, results are mixed. High-quality studies are still needed before a conclusion may be made.

C

Depression

Folic acid deficiency has been found among people with depression and has been linked to poor response to treatment. Folate supplements have been used for enhancing treatment response to antidepressants. Limited research suggests that folic acid may lack effectiveness when compared to standard treatment. Depression should be treated by a qualified healthcare provider.

C

Diabetes

The effect of folic acid on diabetes is not clear. High-quality research is still needed in this area.

C

Down's syndrome

Early research shows a lack of protective effect of folic acid on heart problems in infants with Down's syndrome. Low folate levels in mothers may be a risk factor for babies with Down's syndrome. Further study is needed.

C

Epilepsy

Early research shows a lack of protective effect of folic acid for epilepsy, a seizure disorder. Further study is needed.

C

General health maintenance

Folic acid has been studied for improving well-being in general in both adults and children. However, more research is needed before a conclusion can be made.

C

Glaucoma (eye disease)

Low levels of folic acid and high homocysteine levels have been linked to an increased risk of glaucoma. However, more research is needed before a conclusion can be made on the effects of folic acid supplementation.

C

Gout

Early evidence suggests that higher intake of folic acid may be linked to a lower risk of gout. More study is needed.

C

Growth

Use of multiple vitamins and minerals has been found to improve growth. The effect of folate alone is not clear.

C

Hearing loss

Folic acid supplementation has been found to benefit hearing loss associated with aging. Low folate levels in the blood may be linked to sudden hearing loss in adults. However, more studies are needed.

C

Heart disease

Homocysteine is considered a significant risk factor for heart disease. Levels of this amino acid may be controlled by B vitamins, including folate. However, more research is needed before a firm conclusion can be made.

C

High blood pressure

Some study suggests that folic acid supplementation may decrease high blood pressure. Further study is needed to confirm these results.

C

High blood pressure associated with pregnancy

A combination therapy, including folate, in women with high blood pressure during pregnancy may benefit both the mother and child. More studies are needed to examine the role of folate alone for this condition.

C

High blood sugar/glucose intolerance

In people with high blood sugar, folic acid in combination with enalapril (a blood pressure medication) resulted in lower blood sugar levels, compared to enalapril alone. More trials are needed before a conclusion may be drawn.

C

H. pylori infection

Early evidence suggests that H. pylori infection and low folic acid levels may not be linked. Further study is needed.

C

Kidney disease (chronic)

Although lowering homocysteine levels with folic acid with or without other B vitamins does not appear to reduce heart disease risk in general populations, heart disease risk may be lowered in people with chronic kidney disease. Further study is needed.

Lometrexol toxicity

C

Results are unclear on the use of folic acid for reducing toxicity from the cancer drug lometrexol. More study is needed.

C

Mouth sores (caused by cancer treatment)

The effect of folate on mouth sores associated with cancer treatment is not clear. Further study is required.

C

Multiple sclerosis

Early evidence shows that people with multiple sclerosis may not have significantly altered folate levels, but may have high homocysteine and low B12 levels. Further study is needed.

C

Phenytoin-induced gingival hyperplasia

Early evidence shows that applying folic acid may help prevent the overgrowth of gum tissue caused by therapy with the anti-seizure drug phenytoin. Taking folic acid by mouth has been found to lack benefit. More research is needed in this area.

C

Pregnancy-related gingivitis (gum disease)

Based on early research, applying folic acid to the gum may improve gum disease in pregnant women. More studies are needed to confirm these results.

C

Prevention of pregnancy complications (other)

Studies have shown that folate intake during pregnancy prevents deficiency and associated anemia in pregnant women. Low folate levels during pregnancy may contribute to birth defects and pregnancy loss. Folate alone or in combination with iron may reduce the incidence of low birth weight. The role of folate supplementation in pregnancy and the prevention of heart problems in the baby have also been reviewed. Further study is needed.

C

Stroke

Study results are mixed for the use of folate in people with stroke. Further research is needed in this area before a strong conclusion may be made.

C

Vein clots

Hyperhomocysteinemia may be associated with thrombosis. One study

analysis indicates that folic acid may have a beneficial effect on hypercoagulable (tendency to have blood clots) pregnant women. However, further study is needed.

C

Vitiligo (irregular white patches on the skin)

Early studies suggest that folic acid and vitamin B12 may improve the symptoms of vitiligo. Further research is needed to confirm these results.

D

Fragile X syndrome (genetic disorder causing mental and learning problems)

Studies have shown that folic acid supplementation lacks effect on symptoms of Fragile X syndrome. Further study is needed.

F

Colorectal cancer

Folate supplementation studies in general have found a lack of effect on colorectal cancer. In addition, an increased risk was reported in people treated for 3-6 years with folic acid.

Uses based on tradition or theory

The below uses are based on tradition or scientific theories. They often have not been thoroughly tested in humans, and safety and effectiveness have not always been proven. Some of these conditions are potentially serious, and should be evaluated by a qualified healthcare provider.

AIDS, anemia (associated with inflammatory bowel disease), anti-aging, appetite stimulation, autism, canker sores, celiac disease, critical illness, Crohn's disease, dental conditions, fistula (abnormal connection between organs), fractures (risk reduction), gastritis (stomach inflammation), genetic damage (X-ray induced chromosomal damage), infertility, inflammatory bowel disease, insomnia, ischemic heart disease (decreased blood supply to the heart), lichen planus (itchy mouth rash), liver disease, macular degeneration (eye disease), mood, myofascial pain (chronic muscle pain), osteoporosis, peripheral neuropathy (damage of peripheral nerves such as toes and fingertips), restless leg syndrome, retinal vein occlusion (blockage of veins in the eye), schizophrenia, sickle cell anemia, spinal cord injury, ulcerative colitis, weight loss.

Interactions

Interactions with Drugs

Folate may lower blood sugar levels. Caution is advised when using medications that may also lower blood sugar. People taking drugs for diabetes by mouth or insulin should be monitored closely by a qualified healthcare professional, including a pharmacist. Medication adjustments may be necessary.

Folate may cause low blood pressure. Caution is advised in people taking drugs that lower blood pressure.

Folate may also interact with agents that promote urination, alcohol, Alzheimer's agents, aminosalicic acid, antacids, antibiotics, anticancer agents, antidepressants, anti-malaria agents, anti-seizure agents, aspirin, birth control, cholestyramine, colestipol, conjugated estrogens, cycloserine, folic acid antagonists, H2 blockers, heart agents, homocysteine-lowering agents, iron, methotrexate, methylprednisolone sodium succinate (Solu-Medrol®), nervous system agents, nitroglycerin, nonsteroidal anti-inflammatories (NSAIDs), omega-3 fatty acids, pancreatic extracts, pemetrexed disodium, pentamidine, phenytoin, proton pump inhibitors, sulfasalazine, sulfonamides, tobacco, trimethoprim, vitamin A, vitamin B12, warfarin, and zinc.

Interactions with Herbs and Dietary Supplements

Folate may lower blood sugar levels. Caution is advised when using herbs or supplements that may also lower blood sugar. Blood glucose levels may require monitoring, and doses may need adjustment.

Folate may cause low blood pressure. Caution is advised in people taking herbs or supplements that lower blood pressure.

Folate may also interact with aged garlic extract, alcohol, Alzheimer's herbs and supplements, antacids, antibacterials, anticancer herbs and supplements, antidepressants, anti-inflammatories, anti-malaria herbs and supplements, antioxidants, anti-seizure herbs and supplements, B vitamins, birth control, green tea, heart herbs and supplements, herbs and supplements that promote urination, homocysteine-lowering herbs and supplements, iron, leaf concentrate, multiple micronutrients, nervous system herbs and supplements, omega-3 fatty acids, pancreatic extracts, phytoestrogens, probiotics, salicylates, vitamin A, vitamin B12, and zinc.

Methodology

This information is based on a systematic review of scientific literature, and was peer-reviewed and edited by contributors to the Natural Standard Research Collaboration (www.naturalstandard.com).

[Monograph methodology](#)

Related terms

I-LV, 5-formyltetrahydrofolate, 5-Methyltetrahydrofolate, B complex vitamin, d,I-LV, folacin, folic acid, folinic acid, Folvite®, heptaglutamyl folic acid, hexaglutamyl folic acid, L-5-methyltetrahydrofolate, levoleucovorin, leucovorin, methyltetrahydrofolate, monoglutamyl folic acid, polyglutamyl folic acid, pteroylglutamic acid, pteroylmonoglutamic acid, pteroylpolyglutamate, vitamin B9, vitamin M.

Safety

The U.S. Food and Drug Administration does not strictly regulate herbs and supplements. There is no guarantee of strength, purity or safety of products, and effects may vary. You should always read product labels. If you have a medical condition, or are taking other drugs, herbs, or supplements, you should speak with a qualified healthcare provider before starting a new therapy. Consult a healthcare provider immediately if you experience side effects.

Allergies

Avoid in people with known allergy or sensitivity to product ingredients in folic acid-containing supplements.

Side Effects and Warnings

Folate is likely safe when added to foods in the following amounts: in breakfast cereals, below 400 micrograms per serving; in infant formula, 4 micrograms per 100 kilocalories of infant formula; in corn grits, 1 milligram per pound; in meal-replacement products, 200-400 micrograms per serving, with the amount depending on whether the food is used once or more than once daily.

Use cautiously if taken above the suggested or maximum daily intake levels.

Folate may cause bitter taste, bloating, blood flow problems (caused by narrowed vessels), breathing difficulty, changes in urine color, confusion, cramps, diarrhea, dizziness, fatigue, gas, hair loss, headache, impaired judgment, increased asthma risk (in children of women taking folic acid during late pregnancy), increased cancer risk, increased seizure frequency, inflammation (such as in the mouth), lung muscle spasms, mood swings (excitability or irritability), nausea, overactivity, psychotic behavior, skin symptoms (flushing, hives, itching, rash, and redness), sleep problems, vivid dreaming, and weight changes.

Folate may cause low blood pressure. Caution is advised in people taking drugs or herbs and supplements that lower blood pressure.

Folate may lower blood sugar levels. Caution is advised in people with diabetes or low blood sugar, and in those taking drugs, herbs, or supplements that affect blood sugar. Blood sugar levels may need to be monitored by a qualified healthcare professional,

including a pharmacist, and medication adjustments may be necessary.

Use cautiously in combination with aspirin or in supplemental doses above the maximum daily intake without the care of a medical professional. Injections of folic acid containing benzyl alcohol should only be used under the care of a doctor.

Use cautiously in people who have or are at risk of anemia, cancer, lung disorders, malaria, nervous system disorders, seizure disorders, skin conditions, and stomach problems.

Avoid using with a combination of B vitamins after heart surgery or in people taking anticancer agents or folic acid antagonists (blockers), unless prescribed by a healthcare professional.

Avoid in people with known allergy or sensitivity to product ingredients in folic acid-containing supplements.

Pregnancy and Breastfeeding

The U.S. Preventive Services Task Force and other groups suggests that all women planning to be pregnant take a daily supplement containing 0.4-0.8 milligrams (400-800 micrograms) of folic acid. It is suggested that all women capable of becoming pregnant consume folate in order to reduce the risk of the fetus developing birth defects.

Folic acid is likely safe to use during breastfeeding under the supervision of a qualified healthcare provider.

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