

L-5-MTHF SAP

Science-based metabolically active folic acid

Folic acid, or folate, is a B vitamin that must be derived from either dietary sources or via supplementation. Folate is necessary for a biochemical process in the body called “methylation” or “one-carbon metabolism.”^[1] This process does not work adequately in a significant number of individuals who have a genetic polymorphism, and it may contribute to a host of different concerns, including neural tube defects, depression, and reduction in red blood cell production.^[1] When the body absorbs folate, it goes through a series of biochemical conversions to become the active form L-5-methyltetrahydrofolate.^[1] If an individual is unable to convert the folate properly, they can end up with a deficiency, even though they are eating foods containing folate. Folate is found in leafy green vegetables, legumes, beans, liver, yeast, and citrus fruits.

ACTIVE INGREDIENTS

Each vegetable capsule contains:

L-Methylfolate
(from L-5-methyltetrahydrofolate, calcium salt). . . . 1 mg

Other ingredients: Vegetable magnesium stearate, silicon dioxide, and microcrystalline cellulose in a vegetable capsule composed of vegetable carbohydrate gum and purified water.

This product is non-GMO.

Contains no: Gluten, soy, wheat, corn, eggs, dairy, yeast, citrus, preservatives, artificial flavour or colour, starch, or sugar.

L-5-MTHF SAP contains 60 capsules per bottle.

DIRECTIONS FOR USE

Adults: Take 1 capsule daily with food or as directed by your healthcare practitioner. If you are taking other medications, take this product a few hours before or after them.

INDICATIONS

L-5-MTHF SAP:

- Helps support red blood cell formation.
- Reduces the risk of neural tube defects if taken prior to and during early pregnancy.
- May help to reduce homocysteine levels.
- May prevent folate deficiency, which can lead to symptoms of depression.

CAUTIONS AND WARNINGS

Folate supplementation can mask a vitamin B₁₂ deficiency; consult a healthcare practitioner if you are uncertain whether or not you are taking adequate vitamin B₁₂.

PURITY, CLEANLINESS, AND STABILITY

All ingredients listed for all **L-5-MTHF SAP** lot numbers have been tested by a third-party laboratory for identity, potency, and purity.

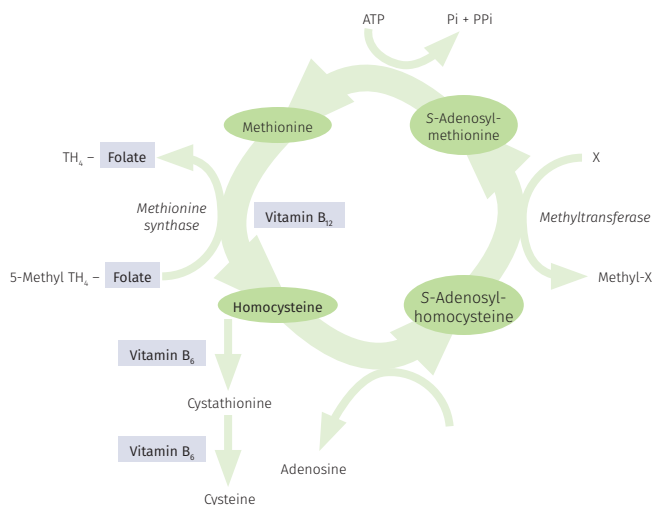


Scientific Advisory Panel (SAP):
adding nutraceutical research
to achieve optimum health



351, Rue Joseph-Carrier, Vaudreuil-Dorion, Quebec, J7V 5V5
T 1 866 510 3123 • F 1 866 510 3130 • nfh.ca

In recent years, there has been a substantial amount of research about folate metabolism, and it is now very apparent that a subset of the population is unable to metabolize folate efficiently.^[1] The enzyme methylenetetrahydrofolate reductase (MTHFR) directs folate either to DNA synthesis or to homocysteine (Hcy) remethylation.^[1] There is a common MTHFR C677T polymorphism which affects the activity of this enzyme, and hence folate distribution, in about 33% of the North American population, where about 10% of the population is homozygous for this mutation.^[1] The impairment that this polymorphism results in is altered folate status. If the patient is homozygous, this has been regarded as harmful, because it is associated with a high concentration of homocysteine, increased risk of neural tube defects, and colorectal neoplasias, and may also predispose individuals to adverse effects from drugs with anti-folate effects.^[1,2]



DEPRESSION

Sufficient levels of folate are critical for healthy brain and body functioning. Folate is required in the brain for synthesis of norepinephrine, serotonin, and dopamine.^[3] There is research supporting that folate deficiency may lead to an increased risk of depression, less than optimal outcomes with antidepressant treatment, as well as increased risk of cognitive impairment.^[3] In North America, folic acid is fortified in several grain products; however, due to genetic polymorphisms absorption and utilization, it is not optimal for several people.^[1] Supplementing with the active form of folate, 5-methyltetrahydrofolate (5-MTHF), may be effective in the prevention and treatment of both depression and dementia.^[3]

There are several different pharmaceutical agents available to treat major depressive disorder (MDD); despite this, many patients experience only mild to modest improvements and low remission rates.^[4] A review article investigating the effect of folate and its efficacy in treating mood disorders discovered some favorable results.^[4] Researchers found that supplementing with various formulations of folates appears to be both well-tolerated and efficacious in reducing depression symptoms.^[4] Researchers also mentioned that supplementing with the bioavailable form 5-MTHF may be a preferable treatment option for MDD in case patients do have a genetic polymorphism hindering their ability to convert folic acid.^[4]

In a double-blind, placebo-controlled study, researchers studied the effect of 5-MTHF supplementation in addition to standard psychotropic medication in depression patients with borderline or definite folate deficiency.^[5] Researchers found that supplementation significantly improved clinical recovery in these patients. Researchers also supplemented elderly depressed patients who had normal folate levels and found improvement in symptoms after three weeks of treatment.^[5] In another arm of the study, researchers assessed the effect of 5-MTHF supplementation on elderly patients with normal folate levels with mild to moderate dementia and depression compared to trazodone.^[5] A total of 96 patients with dementia, who had scored between 12 and 23 on the Mini Mental State Examination and/or ≥ 18 on the Hamilton Depression Rating Scale (HDRS) were included

in the study. After a 2-week placebo run-in, patients were divided into two groups and received either 5-MTHF at 50 mg/d or trazodone at 100 mg/d for eight weeks.^[5] At the end of eight weeks, patients' HDRS score in the 5-MTHF group reduced from 23 ± 3 to 18 ± 6 , and in the trazodone group from 23 ± 3 to 19 ± 5 .^[5]

HOMOCYSTEINE AND VASCULAR DISEASE

An elevated total plasma homocysteine is a risk factor for vascular disease as well as adverse pregnancy outcomes. Excessive intake of folic acid, though, can mask an undiagnosed vitamin B₁₂ deficiency.^[6] The biologically active 5-MTHF may be a viable alternative to folic acid, because it is unlikely to mask vitamin B₁₂ deficiency symptoms.^[6]

In a double-blind, randomized study, researchers looked at the outcome of supplementing either folic acid or 5-MTHF or placebo on tHcy levels.^[6] A total of 144 female patients were divided into four groups and received 400 mcg folic acid, 416 mcg 5-MTHF, 208 mcg 5-MTHF, or placebo.^[6] The concentration of tHcy and plasma folate was measured at baseline and at four-week intervals.^[6] All three treatment groups saw a decrease in tHcy and did not differ significantly. The increase in plasma folate was significantly lower in the group receiving 208 mcg 5-MTHF.^[6] Researchers concluded that 5-MTHF was an adequate alternative to folic acid for tHcy reductions and, for this purpose, 208 mcg and 416 mcg of 5-MTHF had similar efficacy.^[6]

L-5-MTHF IN PREGNANCY

There is a significant body of research that suggests improving folate status periconceptionally reduces the risk of neonatal neural-tube defects.^[7] Therefore, increased folate intake is currently recommended before and during the early stages of pregnancy.^[7] Folic acid in its synthetic form (which is only found in supplements and fortified foods) lacks the coenzyme activity and must be reduced to its metabolically active form L-5-methyltetrahydrofolate within the cell.^[7] L-5-methyltetrahydrofolate is the predominant form of dietary folate and the only species normally found in circulation; therefore, it is the form that is normally transported into peripheral tissues and used for cellular metabolism.^[7] Studies comparing folic acid to L-5-methyltetrahydrofolate have found that both compounds are comparable in terms of physiological activity, bioavailability, and absorption.^[7] Supplementing with the L-5-methyltetrahydrofolate form may have an advantage over folic acid, because it is the form found in circulation and is associated with a reduced interaction with drugs that inhibit dihydrofolate reductase; also, there is less masking of the hematological symptoms of a vitamin B₁₂ deficiency.^[7]

L-5-Methyltetrahydrofolate is the most active form of folate found in plasma, and it is able to directly enter the metabolic process.^[8] Compared to folic acid, L-5-methyltetrahydrofolate shows optimum absorption as well as comparable or higher bioavailability and physiological activity.^[8] L-5-Methyltetrahydrofolate supplementation is effective at decreasing plasma homocysteine and in increasing folate in both plasma and erythrocytes in women who were pregnant, breast-feeding, or trying to conceive.^[8] There have been no reported adverse or toxic effects of supplementation with 5-MTHF. Based on current literature, 5-MTHF could be an effective and safe alternative to folic acid supplementation and could effectively prevent birth defects and pregnancy complications.^[8]

REFERENCES

- Ueland, M., et al. "Biological and clinical implications of the MTHFR C677T polymorphism." *Trends in Pharmacological Science* Vol. 22, Issue 4 (2001): 195-201.
- <http://lpi.oregonstate.edu/infocenter/vitamins/fa/> · Accessed August 12, 2014
- Fava, M. and D. Mischoulon. "Folate in depression: efficacy, safety, differences in formulations, and clinical issues." *The Journal of Clinical Psychiatry* Vol. 70, Suppl. 5 (2009): 12-17.
- Papakostas, G.I., C.F. Cassiello, and N. Iovieno. "Folates and S-adenosylmethionine for major depressive disorder." *Canadian Journal of Psychiatry* Vol. 57, No. 7 (2012): 406-413.
- Passeri, M., et al. "Oral 5'-methyltetrahydrofolic acid in senile organic mental disorders with depression: results of a double-blind multicenter study." *Aging (Milano)* Vol. 5, No. 1 (1993): 63-71.
- Lamers, Y., et al. "Supplementation with [6S]-5-methyltetrahydrofolate or folic acid equally reduces plasma total homocysteine concentrations in healthy women." *The American Journal of Clinical Nutrition* Vol. 79, No. 3 (2004): 473-478.
- Pietrzik, K., L. Bailey, and B. Shane. "Folic acid and L-5-methyltetrahydrofolate: comparison of clinical pharmacokinetics and pharmacodynamics." *Clinical Pharmacokinetics* Vol. 49, No. 8 (2010): 535-48.
- Seremak-Mrozikiewicz, A. "[Metafolin – alternative for folate deficiency supplementation in pregnant women]" (article in Polish). *Ginekologia Polska* Vol. 84, No. 7 (2013): 641-646.