L-5-MTHF provides folate in a bioidentical, bioactive form, 5-methyltetrahydrofolate. L-5-MTHF (the “L” signifying that it is the all-natural [6S] isomer) is the active circulating form of folate found in the body and one of the several forms found in food. In nature it is found only as this [6S] isomer, which is why DFH provides 5-MTHF in this natural form rather than the mixed (or racemic) form. L-5-MTHF was designed for patients with demonstrated increased need for folate, such as those with either the A1298C or C677T MTHFR mutation.

Our L-5-MTHF uses the patented folate derivative Quatrefolic®. This innovative form of folate has demonstrated high bioavailability and solubility as well as long lasting stability. Quatrefolic® L-5-MTHF helps to increase blood folate levels much better than folic acid.

Folate and Human Health

Folate is one of the most essential nutrients needed during rapid cell division and growth. It is no surprise that pregnancy doubles the need for dietary folates. Folate coenzymes play a vital role in metabolism through two different pathways: the synthesis of DNA from its precursors (purines/thymidines) and the homocysteine (methionine) pathway. 5-MTHF is needed for the conversion of homocysteine to methionine which allows for the production of S-adenosylmethionine (known as SAMe). The importance of this is that SAMe is the universal methyl donor. Methyl-group donation is vital to proper cell replication and differentiation, and to many biochemical conversion processes, including the synthesis of serotonin, melatonin, and DNA.

Folate vs. Folic Acid

While folates are naturally occurring in food, folic acid is a fully oxidized, synthetic compound (pteroylmonoglutamic acid) used in most dietary supplements and in food fortification, but is not found in nature. Designs for Health uses only natural folates found in food rather than folic acid. Due to enzyme defects or deficiencies, many people do not properly convert folic acid into natural folates including 5-MTHF.

Although folic acid has been associated with several health benefits, such as reduction of neural tube defects and homocysteine, 5-MTHF supplementation would be a better way to reap these benefits since it is already activated and not associated with high levels of unmetabolized folic acid in the blood, as unmetabolized folic acid is implicated in an increase in the number of cancer deaths in the US. New research has emerged raising concern over the safety of chronic intake of high levels of folic acid from fortified foods, beverages, and dietary supplements.

The MTHF Reductase enzyme, or MTHFR, plays a prominent role in the homocysteine pathway, a chemical reaction involving folates. One of this enzyme’s functions is to process homocysteine, changing it to methionine which is then used to make SAMe, the most important methyl donor in the body. To be more specific, reduction of 5,10-methylenetetrahydrofolate (methyleneTHF) to 5-methyltetrahydrofolate (methylTHF), the primary methyl donor for methionine synthesis, is catalyzed by the MTHFR enzyme. See diagram above.
Having a mutation in the *MTHFR* gene impacts how well the MTHFR enzyme performs. A MTHFR deficiency may lead to hyperhomocysteinemia. There are several MTHFR gene mutations which result in a mild to severe impairment of the activity of the MTHFR enzyme, the most characterized mutation being C677T (C677T MTHFR mutation).

This gene mutation makes a patient more susceptible to:

- coronary heart disease
- stroke
- preeclampsia (high blood pressure in pregnant women)
- birth defects including neural tube defects
- suboptimal methylation issues

Methylation issues caused by this gene mutation are due to a decrease in SAMe production, again the body’s primary methyl donor. Research studies have correlated this with demyelination of the brain and spinal cord.

### L-5-MTHF should be considered when high doses of folate are needed

Individuals who have tested homozygous with either the A1298C or C677T MTHFR mutation, or those with elevated homocysteine levels, should be using L-5-MTHF as the preferred form of folate supplementation. This may be more effective for them than other forms of folic acid or folates.

**Others who may benefit from L-5-MTHF:**

- pregnant women and women wishing to become pregnant who have familial history of depression, high homocysteine levels, or genetic defect in MTHFR. *Note: All pregnant women should consider taking Prenatal Pro™ as their comprehensive multivitamin, which can be combined with L-5-MTHF if higher levels of folate are needed.*
- women with abnormal pap smears (precancerous)
- those with very high homocysteine levels not responding quickly to Homocysteine Supreme™ (consider using them together)
- dialysis patients
- organic acid testing (as included in the DFH metabolic profiles) that reveals elevated FIGLU (marker used to identify folate deficiency)
- patients with family history of dementia/vascular dementia
- patients with depression
- long-term alcoholism
- long-term use of oral contraceptives
- persistent use of the following medications known to lower folate levels:
  - high doses of NSAIDs (i.e., ibuprofen and aspirin)
  - anticonvulsants: phenytoin, phenobarbital, and primidone
  - trimethoprim (antibiotic), pyrimethamine (antimalarial), triamterene (blood pressure medication), and sulfasalazine (treatment for ulcerative colitis)

Do not take 5-MTHF simultaneously with the cholesterol-lowering agents cholestyramine or colestipol because they may decrease the absorption of folate.

**Related resource material:**

Access related articles in the DFH Response to the Folic Acid Controversy located in the library section of our website.

*For a list of references cited in this document, click the related research link on the product landing page at http://mkt.s.designsforhealth.com/techsheets/L5-MTHF_references.pdf*