

5-Methyl Folate

TECHNICAL SUMMARY

Folate consumed in the diet or from supplements must be converted to its active form, 5-Methyltetrahydrofolate (5-MTHF), to be used by the body. This is a multi-step biochemical process that, in some circumstances, may not be efficient enough to meet the body's needs. In addition, unlike folic acid, 5-MTHF can penetrate the blood-brain barrier. This product utilizes a patented form of 5-MTHF with superior bioavailability.

Structure Formula:

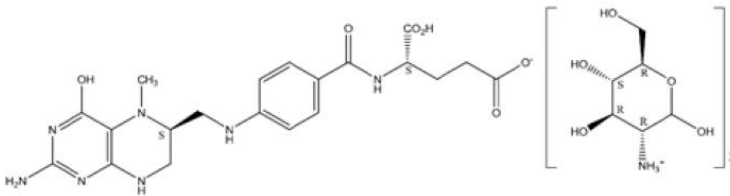


Figure 1: Chemical structure of 5-MTHF Glucosamine Salt

Chemical Name: (6S)-5-Methyltetrahydrofolic Acid Glucosamine Salt

Allergen and Additive Disclosure: Not manufactured with wheat, gluten, soy, milk, egg, fish, shellfish or tree nut ingredients. Non-GMO corn-derived ingredient in formula. Produced in a GMP facility that processes other ingredients containing these allergens. Vegetarian friendly product.

Delivery Form: Tablets

ROLE AS NUTRIENT/FUNCTION

5-MTHF is the predominant folate form entering human metabolism and the transport form of folate in plasma.* Folate coenzymes, including 5-MTHF, are involved in three major interrelated metabolic cycles.* These cycles are required for the synthesis of thymine and purines (precursors of DNA and RNA), for recycling homocysteine, and for the interconversion of serine and glycine.* 5-MTHF is particularly involved in the conversion of homocysteine to methionine; this reaction also needs zinc and vitamin B₁₂ as cofactors.* Methionine can then be metabolized to S-adenosylmethionine which is involved in the methylation of DNA, proteins, neurotransmitters, phospholipids, and the synthesis of creatine.* This methylation cycle is very sensitive to folate status, since a deficit in 5-MTHF will result in a rise in plasma homocysteine level.*

NATUROKINETICS®

Liberation: 5-Methyl Folate Tablets pass the standard disintegration test in water (<60 minutes). After oral ingestion, 5-MTHF and the glucosamine salt dissociate rapidly in the aqueous environment of the digestive tract.

Absorption: 5-MTHF is absorbed in the proximal small intestine via the proton-coupled folate transporter. When folic acid is administered orally, it must be reduced and converted to 5-MTF before being absorbed. Because 5-MTHF does not require this initial metabolic step, it results in higher bioavailability when taken orally. Clinical data from a phase I clinical study on healthy volunteers suggest that glucosamine salts of 5-

Supplement Facts

Serving Size 1 Tablet

	Amount Per Serving	%Daily Value
Folate	1,667 mcg DFE	417%
	[1,000 mcg (6S)-5-MTHF**]	
	[from Quatrefolic® (6S)-5-MTHF** Glucosamine Salt]	

Other ingredients: Cellulose, Stearic Acid (vegetable source) and Silica.

- **Metabolically Active Folate***
- **Superior Bioavailability**

SUGGESTED USAGE: Take 1 tablet daily with a meal, or as directed by your healthcare practitioner.

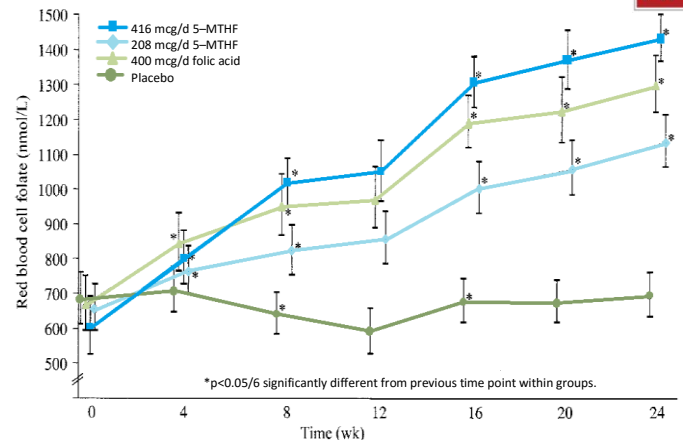


Figure 2: Mean RBC folate concentration after 24 weeks supplementation in healthy women

MTHF have a 10% increased bioavailability when compared to calcium salts of 5-MTHF.

Distribution: In blood, 5-MTHF circulates in its free form or loosely bound to plasma proteins (albumin) and red blood cells, which contain higher levels of folate than plasma, largely as 5-MTHF polyglutamates. At the tissue level, there is a complex homeostatic mechanism using different transporters and receptors that prevent the accumulation of excessive levels of folate in tissues, even when plasma folate concentrations are high. 5-MTHF is transported into most peripheral tissues via reduced folate carrier-1 (RFC1) or the proton-coupled folate transporter (PCFT) or Folate Receptor α (FR α). FR α is known to have a higher affinity for 5-MTHF. In the brain, 5-MTHF transport into the central nervous system takes place across the choroid plexus, where both FR α and RFC1 are involved in this active transport process. This results in a two- to three-fold greater concentration of 5-MTF in the cerebrospinal fluid when compared to the blood. A double-blind, randomized, placebo-controlled

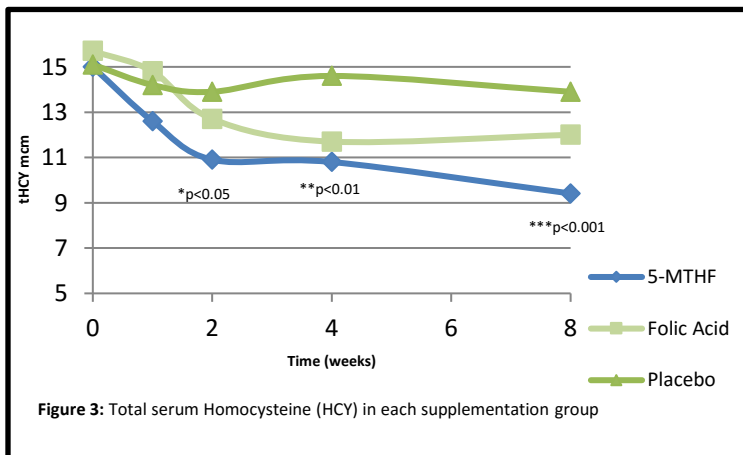
clinical study evaluating the effect of daily supplementation with 400 mcg folic acid vs. an equimolar amount of 5-MTHF (416 mcg) or 208 mcg 5-MTHF for 24 weeks on red blood cell (RBC) folate in healthy women demonstrated a significantly greater increase in RBC folate in the 416 mcg/d 5-MTHF group.* (Figure 2)

Metabolism: 5-MTHF metabolism is detailed in the structural/functional role section above.

Elimination: 5-MTHF is excreted mainly in the bile and also in the urine especially when plasma concentration exceeds 45 nmol/L.

CLINICAL VALIDATION

- A double-blind, randomized, placebo-controlled clinical study evaluating the effect of a daily supplementation of 1 g folic acid vs. 1 g 5-MTHF for 8 weeks in 48 adults demonstrated significant support of normal total serum homocysteine levels in the 5-MTHF group as early as week 2, and were maintained for the duration of the supplementation (statistically significant compared to baseline)* (Figure 3).



SAFETY INFORMATION

Tolerability: 5-MTHF is generally well tolerated. There have been some concerns that high folate supplementation may mask symptoms of vitamin B₁₂ deficiency, especially in elderly populations. It is recommended to test for pernicious anemia in elderly individuals and individuals at known risk of vitamin B₁₂ deficiency before implementing supplementation with 5-MTHF.

Contraindications: None

INTERACTIONS

Drug Interactions: Probable interactions with phenytoin, fosphenytoin, methotrexate, phenobarbital, and primidone.

Supplement Interactions: Tea may interact with folate absorption.

Interaction with Lab Tests: Mean corpuscular volume (MCV), folate supplementation can normalize megaloblastic anemia due to vitamin B₁₂ deficiency.

STORAGE

Store in a cool, dry place in a sealed container. Protect from excessive heat and moisture.