

## METHYL-ACTION

### TECHNICAL SUMMARY

Methyl-Action is formulated to support essential methylation with B-vitamins in their active forms.\* Healthy methylation is vital for normal homocysteine metabolism.\* Maintaining normal homocysteine levels promotes neurological, cardiovascular, eye, and bone health.\*

**Biochemistry:** Methyl-Action has a balanced combination of B vitamins in their activated co-enzyme states combined with betaine anhydrous also known as trimethylglycine (TMG).

**Allergen and Additive Disclosure:** Not manufactured with wheat, gluten, soy, milk, egg, fish, shellfish, tree nut or sesame ingredients. Produced in a GMP facility that processes other ingredients containing these allergens.

**Delivery Form:** Vegetable capsules.

### ROLE AS NUTRIENT/FUNCTION

B vitamins are required as co-enzymes for numerous complex reactions that are essential to cellular function and energy production, notably at the mitochondrial level.\* Some of the systems in which B vitamins function can be summarized as follows:

- Riboflavin: cellular respiratory chain, energy metabolism, metabolism of neurotransmitters\*
- Vitamins B<sub>6</sub> and B<sub>12</sub>: cellular energy production, glutathione and nucleotides biosynthesis, homocysteine recycling\*
- Folate: biosynthesis of nucleotides and S-adenosylmethionine (SAMe)\*
- Betaine: essential component of the methionine/homocysteine cycle. As methyl group donor it helps recycle homocysteine and support healthy liver function.\* It also helps to maintain intercellular osmolarity and protects proteins from denaturation.\* Betaine is endogenously produced by the oxidation of choline.<sup>1\*</sup>

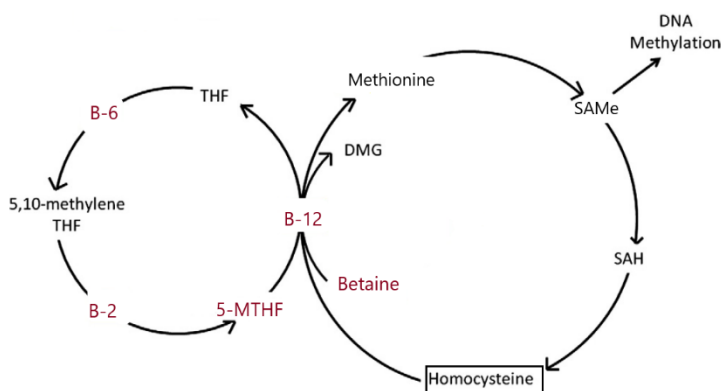


Figure 1: Involvement of Methyl-Action ingredients in one-carbon metabolism. (In red). (1) Vitamin B<sub>2</sub> is a precursor to flavin adenine dinucleotide (FAD), which is a cofactor to methylenetetrahydrofolate reductase (MTHFR) in the conversion of 5,10-methylene tetrahydrofolate (THF) to 5-MTHF. (2) Vitamin B<sub>6</sub> is a cofactor for serine

## Supplement Facts

Serving Size 2 Veg Capsules  
Servings Per Container 45

	Amount Per Serving	% Daily Value
Riboflavin (Vitamin B-2) (from Riboflavin-5-Phosphate Sodium)	25 mg	1923%
Vitamin B-6 (from Pyridoxal-5-Phosphate Monohydrate)	25 mg	1471%
Folate [588 mcg (6S)-5-MTHF**] [from Quatrefolic® (6S)-5-MTHF** Glucosamine Salt]	1,000 mcg DFE	250%
Vitamin B-12 (as Methylcobalamin)	1,000 mcg	41,667%
Trimethylglycine (TMG) (Betaine Anhydrous)	1,000 mg	†

† Daily Value not established.

Other ingredients: Hypromellose (cellulose capsule), Microcrystalline Cellulose, Stearic Acid (vegetable source) and Silicon Dioxide.

- **Methylation Support\***
- **B-vitamins in Active Forms**
- **Helps Maintain Homocysteine Levels Already Within the Normal Range\***

**SUGGESTED USAGE:** Take 2 capsules daily, or as directed by your healthcare practitioner.

hydroxymethyltransferase in the conversion of THF to 5,10-methylene THF. (3) Vitamin B<sub>12</sub> is a precursor to methionine synthase, which is involved in the production of methionine from homocysteine and betaine.

### NATUROKINETICS®

**Liberation:** This product passes standard USP disintegration test in water in no more than 60 minutes.

**Absorption:** B vitamins are absorbed in various parts of the intestine via several different mechanisms.

**B<sub>2</sub>:** Absorption of dietary riboflavin occurs through a saturable, proximal small intestinal transport system. Absorption is increased with food and delayed on empty stomach. Some riboflavin is also absorbed in the colon.

**B<sub>6</sub>:** Pyridoxal 5-phosphate (PLP) is dephosphorylated by an intestinal phosphatase, prior to absorption from the upper small intestine by a carrier-mediated system.

**(6S)-5-MTHF:** (6S)-5-MTHF is absorbed in the small intestine by an active carrier-mediated transport as well as by passive diffusion in the colon. Preclinical and clinical studies have shown that Quatrefolic® has a higher bioavailability than folic acid and calcium salt of (6S)-5-MTHF.

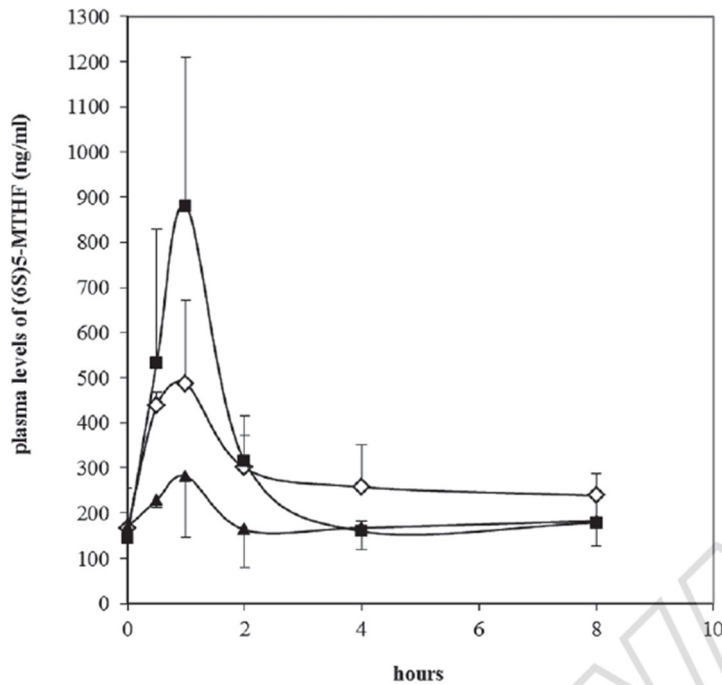


Figure 2: plasma concentration of (6S)-5-MTHF in rats receiving 70 mcg/kg (6S)-5-MTHF equivalents of folic acid (black triangles), (6S)-5-MTHF Ca salt (white diamond) or Quatrefolic®(black square). Adapted from Miraglia et al.

**B<sub>12</sub>:** While vitamin B<sub>12</sub> is absorbed in the small intestine, it requires intrinsic factor (IF) from the stomach to facilitate its absorption, as well as a properly functioning pancreas. At larger doses, such as those included in this product, B<sub>12</sub> is passively absorbed in the intestine without IF in a non-saturable manner; this passive absorption typically represents 1% of the ingested dose.

**TMG:** After ingestion betaine is rapidly absorbed with a peak concentration being reached in less than one hour.

**Distribution:** B vitamin distribution in the body differs depending on the vitamin. For example, the body has limited storage capacity for riboflavin; however, it is found in most tissues with greater amounts in the liver, heart and kidneys, and to a lesser extent in the blood.

Albumin-bound PLP represents about 60% of circulating vitamin B<sub>6</sub>. B<sub>6</sub> is mainly stored in muscle tissue, and to a lesser extent in the liver. While dephosphorylated B<sub>6</sub> vitamers can enter cells and pass the blood-brain barrier, circulating PLP needs to be dephosphorylated by tissue-specific phosphatases or tissue-nonspecific alkaline phosphatases (TNAP) to enter cells.

Folate stores are small, with half of the body store of folate in the liver. Folate is present in all cells of the body as it is essential to cell survival.

B<sub>12</sub> is mainly stored in the liver but is also present in red blood cells, kidneys, muscle, bones, and the brain.

Betaine is distributed throughout the body.

**Metabolism:** B vitamin metabolism is complex and follows different pathways.

Riboflavin is metabolized to flavin mononucleotide (FMN), which can be used to form some flavoproteins, but it is mainly converted to flavin

adenine dinucleotide (FAD), the predominant flavo-coenzyme in body tissues.

Vitamin B<sub>6</sub> (B<sub>6</sub>) comprises a group of six related compounds: pyridoxal (PL), pyridoxine (PN), pyridoxamine (PM), and their respective 5'-phosphates [PLP, PNP, and PMP]. Most of the absorbed non-phosphorylated B<sub>6</sub> goes to the liver where PN, PL, and PM are converted to PNP, PLP, and PMP by PL kinase. PNP and PMP are oxidized to PLP by PNP oxidase. PMP is also generated from PLP via aminotransferase reactions. PLP can be oxidized to 4-pyridoxic acid (4-PA), which is released by the liver and excreted in urine.

Folate metabolism, which is an integral part of its function, is complex and requires other B vitamins including vitamins B<sub>6</sub>, B<sub>12</sub>, and NADP (a niacin derivative). Folate is essential for metabolic pathways involving cell growth, replication and survival.

In cells, B<sub>12</sub> is extensively metabolized by a series of proteins.

Betaine is extensively metabolized into dimethylglycine (DMG), the biochemical reaction requires vitamin B<sub>12</sub> to occur.

**Elimination:** B vitamins are eliminated in urine. Riboflavin, and B<sub>12</sub> are also eliminated through the bile. B<sub>12</sub> is then partially reabsorbed in the intestine; the non-reabsorbed portion is eliminated in feces. Most of the folate excreted in the kidneys is reabsorbed in the proximal renal tubule.

For betaine, the elimination half-life is 14 hours after a single ingestion and up to 41 hours after repeated ingestion over a 5-day period. Due to its extensive metabolism into DMG, only 4% of ingested betaine is eliminated in urine.

### CLINICAL VALIDATION

- In a 2-year, randomized, placebo-controlled study, 156 healthy elderly volunteers with memory complaints received B-vitamin supplementation (folic acid 0.8 mg/d, vitamin B<sub>12</sub> 0.5 mg/d, vitamin B<sub>6</sub> 20 mg/d) or placebo. At the end of the supplementation period, volunteers from the vitamin B group showed significantly less atrophy of grey matter (GM) vs. placebo group in posterior regions of the brain.

### SAFETY INFORMATION

**Tolerability:** The tolerability of this specific blend of ingredients has not been clinically evaluated; however, B vitamins, even at large daily doses, are typically well tolerated.

**Contraindications:** None known.

### INTERACTIONS

Drug interactions, supplement interactions and interaction with lab tests have not been clinically evaluated for this specific blend of ingredients.

### STORAGE

Store in cool, dry environment in original tightly sealed container.