



## Formula Ingredient And Peer Reviewed Supportive References:

### Folate (5-methyltetrahydrofolate and Folinic Acid)

Active forms of folate, such as 5-methyltetrahydrofolate, and folinic acid, play one of the most pivotal roles in keeping the nervous system, cardiovascular system, detoxification system, and DNA repair system working optimally. The blend of folates in Complete Methylation Support was critically chosen due to their distinct roles in human health and development. Folate is a nutrient that has to be reduced, or broken down, for the body to utilize it in effective ways. Over half of the population has genetic mutations that prevent the conversion of folate, which can result in high levels of homocysteine (2). Homocysteine in high amounts is correlated with depressive disorders in addition to acting as a toxicant to blood vessels, damaging the structure of the vasculature, which then prompts the body to build unwanted plaque to repair that damage (15). This is why it is critical to clear unwanted high levels of homocysteine, which can be supported through use of reduced folates and bioactive B vitamin cofactors (1,7). Folinic acid is often left out of supplement formulations, neglecting this unique form of folate that is essential for many processes in the body such as DNA and gene regulation (9). For growing and developing children, this is especially a critical form of reduced folate, for it has been demonstrated that folinic acid can improve speech and language in children and also reduce symptoms of autism (5,6). In adults, folinic acid has been shown to improve cognitive function (IQ) and memory, in addition to improving cardiovascular endothelial function (blood vessel health) (4,11). Folinic acid also has a compelling role in helping support patients that are going through cancer treatments (helping rescue cells that have become toxic from cancer therapies), however this is managed through a medical provider, with a prescription medication (which is simply folinic acid) called Leucovorin (10). Folate and B12 deficiency has been demonstrated as a correlative factor in depression (8,12). Studies have shown taking folate with antidepressant medications can improve treatment response to major depressive disorders (3,14). In fact, mental health providers often use prescription forms of folate (the same ingredient used in Complete Methylation Support and Mood Support) such as Deplin or Enlyte, as a single agent to treat depression or as an adjunctive agent to improve depression treatment response (16). In addition, other B vitamins, such as B6, B2, and B12, which are

included in Complete Methylation Support, are essential co factors that can promote normalization and balance of neurotransmitter production (serotonin, dopamine, norepinephrine, epinephrine, and GABA) (12,13).

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## Vitamin B12 (Methylcobalamin and Hydroxocobalamin)

Vitamin B12 is required for the development of the nervous system, to make healthy red blood cells, and to support DNA synthesis and repair (which is critical for growth and development in children) (2). B12 also helps keep the amino acid, homocysteine, in balance. High levels of homocysteine in the body causes stress on the cardiovascular system in addition to impaired methylation and impaired detoxification. When the body is lacking an optimal amount of B12, problems such as pernicious anemia, chronic fatigue, developmental delays, mood disorders, high homocysteine, and more can evolve. Deficiencies in B12 are common, especially in those individuals taking antacids or blood sugar

medications, have gut dysfunction, are elderly, or are on a vegetarian or vegan diet. Genetic mutations in B12 genes are also important contributing factors to how B12 is absorbed into the body and the brain. Mutations can include ways the body breaks B12 down, metabolizes it, absorbs it into the gut, transports to the brain and other tissues, and utilizes it for mitochondrial function. The body does not produce B12 on its own, and this nutrient must be acquired from sources outside the body, such as through food or supplementation. The bioavailability of B12 is 50X higher when taken in supplemental form (2). There is no upper tolerable limit with dosing established for B12 by the US government because B12 is considered safe, is not stored in the body (so what is not utilized is excreted), and it has a low potential for toxicity. We chose two types of B12 for Complete Methylation Support due to their unique functions. Hydroxycobalamin binds to transcobalamins, enhancing transport to tissues, which can be especially helpful in those with genetic transport mutations (1). Methylcobalamin is the most active form of B12 and does not have to be broken down in the body to be used by the nervous system. Both methylcobalamin and hydroxycobalamin have been studied in children with developmental delay and autism, and found to improve metabolic dysfunction as well as decrease autistic symptoms (3).

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## Vitamin B2 or Riboflavin (Riboflavin-5-Phosphate)

Vitamin B2, otherwise known as riboflavin, is a vital cofactor to produce enzymes that help our bodies make energy (via ATP production) (2). Deficiencies in riboflavin can be a contributing factor in mitochondrial dysfunction and headaches (1). Riboflavin has been shown to support DNA methylation in individuals with genetic mutations in their folate reducing genes (specifically MTHFR) (3). Riboflavin also plays a role in lowering homocysteine and supporting healthy methylation.

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## Vitamin B6 (Pyridoxine HCl)

Vitamin B6 is a water soluble B vitamin that supports over 140 enzyme functions in the body. B6 plays a critical role in the regulation of the nervous system by facilitating the development of neurotransmitters, such as GABA, serotonin, and dopamine (1). There are genetic mutations in humans that can impair the way B6 is metabolized in the body, such as rapid clearance or inactivation, leading to lower levels of bioavailability (2,6). Deficiencies in B6 have been correlated with seizure disorders, high homocysteine (impaired methylation), autism, depression, MSG reactivity, carpal tunnel syndrome, cardiovascular disease, kidney stones, and asthma (3). Taking exceedingly high levels of B6 (>1,000mg/day) can lead to toxicity over time, however this is rare. In Complete Methylation Support, the dose of B6 is well within the upper tolerable limit according to the National Institute of Health (4). Children 1-3 years should stay under 30mg of B6 daily, 4-8 years 40mg daily, 9-13 years 60mg daily, 14-18 years 80mg daily, and 19+ years 100mg daily. These guidelines were established with the general population, and do not take individual genetic variances into account (which could infer a need for higher daily doses, even outside of published limits).

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