



# Complete Methylation Support

Bioactive B Vitamins



## Directions:

Take 1-2 capsules daily or as directed by your health care provider

**Serving Size: 1 capsule**

## Ingredients:

Riboflavin (Riboflavin 5 Phosphate) 20.00 mg, Folate (L-5-methyltetrahydrofolate, calcium salt) 3000.00 mcg, Folate (Folinic Acid) 2000.00 mcg, Vitamin B-12 (Methylcobalamin) 1000.00 mcg, Vitamin B-6 (Pyridoxal 5-Phosphate) 25.00 mg

## Clinical Applications:

- Promotes a healthy mood and reduction in depressive symptoms
- Supports growth, speech, and language development in children
- Enhances cognitive function and memory
- Promotes healthy gene regulation and DNA repair
- Enhances antidepressant medication efficacy
- Supports clearance of toxic high levels of homocysteine
- Promotes healthy cardiovascular function

## Description:

Easy to swallow capsules designed to support healthy function of the nervous system, cardiovascular system, growth and development in children, and balance of healthy biochemistry. The blend of ingredients in this product are specifically designed in therapeutic amounts, based on peer reviewed clinical evidence, and years of clinical experience, to promote and enhance optimal health, development, and methylation.

**Disclaimer:** These statements have not been evaluated by the Food and Drug Administration. Our products are not intended to diagnose, treat, cure, or prevent any disease.

©2024 Neuro Nutrients® - Do not copy. All rights reserved.

**512.599.8851** | [www.neuronutrients.com](http://www.neuronutrients.com)  
4131 Spicewood Springs Rd, Bldg A - Ste #8  
Austin, TX 78759

**Suggested Use:** Take 1-2 capsules daily or as directed by your health care provider.

Store in a cool, dry place with the lid tightly closed. Keep out of reach of children.

**WARNING:** Consult your health care provider prior to using this product if you are pregnant, nursing, taking medication or have a medical condition.

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

**Manufactured For:**  
 Neuro Nutrients  
 4131 Spicewood Springs Rd.  
 Bldg A, #8  
 Austin, TX 78759  
 (512) 599-8851



Made in a GMP Certified Facility in the U.S.



## Complete Methylation Support

Bioactive B Vitamins

*Small and easy to swallow capsules!*

Dietary Supplement

60 Capsules

## Supplement Facts

Serving Size 1 Capsule  
 Servings Per Container 60

	Amount Per Serving	%DV
Riboflavin (as Riboflavin 5'-Phosphate)	20mg	1538%
Vitamin B6 (as Pyridoxal 5'-Phosphate)	25mg	1471%
Folate (60% as 5-MTHF, calcium salt, 40% as Folinic Acid)	8500 mcg DFE (5100 mcg)	2125%
Vitamin B12 (as Methylcobalamin)	1000 mcg	41667%

† Daily Value (DV) not established

Other ingredients: Microcrystalline Cellulose (USP), Vegetable Capsule (cellulose, purified water)

Wheat Free, Dairy Free, Free of Artificial Colors/Flavors, Egg Free, Shellfish Free, Tree Nut Free, Peanut Free

## 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

**Disclaimer:** These statements have not been evaluated by the Food and Drug Administration. Our products are not intended to diagnose, treat, cure, or prevent any disease.

512.599.8851 | [www.neuronutrients.com](http://www.neuronutrients.com)  
 4131 Spicewood Springs Rd, Bldg A - Ste #8

©2024 Neuro Nutrients® - Do not copy. All rights reserved.

Austin, TX 78759

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).

---

1. Chung, K. H., Chiou, H. Y., & Chen, Y. H. (2017). Associations between serum homocysteine levels and anxiety and depression among children and adolescents in Taiwan. *Scientific reports*, 7(1), 8330. <https://doi.org/10.1038/s41598-017-08568-9>
2. Clifford AJ, Chen K, McWade L, et al. Gender and Single Nucleotide Polymorphisms in MTHFR, BHMT, SPTLC1, CRBP2, CETP, and SCARB1 Are Significant Predictors of Plasma Homocysteine Normalized by RBC Folate in Healthy Adults. *J Nutr*. 2012;142(9):1764-1771. doi:10.3945/jn.112.160333
3. Coppen A, Bailey J. Enhancement of the antidepressant action of fluoxetine by folic acid: a randomised, placebo controlled trial. *J Affect Disord*. 2000 Nov;60(2):121-30. doi: 10.1016/s0165-0327(00)00153-1. PMID: 10967371.
4. De Jager CA, Oulhaj A, Jacoby R, Refsum H, Smith AD. Cognitive and clinical outcomes of homocysteine-lowering B-vitamin treatment in mild cognitive impairment: a randomized controlled trial. *Int J Geriatr Psychiatry*. 2012 Jun;27(6):592-600. doi: 10.1002/gps.2758. Epub 2011 Jul 21. PMID: 21780182.
5. Frye RE, Melnyk S, Fuchs G, Reid T, Jernigan S, Pavliv O, Hubanks A, Gaylor DW, Walters L, James SJ. Effectiveness of methylcobalamin and folinic Acid treatment on adaptive behavior in children with autistic disorder is related to glutathione redox status. *Autism Res Treat*. 2013;2013:609705. doi: 10.1155/2013/609705. Epub 2013 Oct 12. PMID: 24224089; PMCID: PMC3810468.
6. Frye, R. E., Slattery, J., Delhey, L., Furgerson, B., Strickland, T., Tippet, M., Sailey, A., Wynne, R., Rose, S., Melnyk, S., Jill James, S., Sequeira, J. M., & Quadros, E. V. (2018). Folinic acid improves verbal communication in children with autism and language impairment: a randomized double-blind placebo-controlled trial. *Molecular psychiatry*, 23(2), 247–256. <https://doi.org/10.1038/mp.2016.168>
7. Ganguly, P., & Alam, S. F. (2015). Role of homocysteine in the development of cardiovascular disease. *Nutrition journal*, 14, 6. <https://doi.org/10.1186/1475-2891-14-6>
8. Gilbody S, Lightfoot T, Sheldon T. Is low folate a risk factor for depression? A meta-analysis and exploration of heterogeneity. *J Epidemiol Community Health*. 2007 Jul;61(7):631-7. doi: 10.1136/jech.2006.050385. PMID: 17568057; PMCID: PMC2465760.
9. Gristan YD, Moosavi L. Folinic Acid. [Updated 2021 Jul 16]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK545232/>

10. Hegde VS, Nagalli S. Leucovorin. [Updated 2021 Nov 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK553114/>
11. McRae MP. High-dose folic acid supplementation effects on endothelial function and blood pressure in hypertensive patients: a meta-analysis of randomized controlled clinical trials. *J Chiropr Med.* 2009 Mar;8(1):15-24. doi: 10.1016/j.jcm.2008.09.001. PMID: 19646382; PMCID: PMC2697578.
12. Mech AW, Farah A. Correlation of clinical response with homocysteine reduction during therapy with reduced B vitamins in patients with MDD who are positive for MTHFR C677T or A1298C polymorphism: a randomized, double-blind, placebo-controlled study. *J Clin Psychiatry.* 2016 May;77(5):668-71. doi: 10.4088/JCP.15m10166. PMID: 27035272.
13. Miller AL. The methylation, neurotransmitter, and antioxidant connections between folate and depression. *Altern Med Rev.* 2008 Sep;13(3):216-26. PMID: 18950248.
14. Passeri M, Cucinotta D, Abate G, Senin U, Ventura A, Stramba Badiale M, Diana R, La Greca P, Le Grazie C. Oral 5'-methyltetrahydrofolic acid in senile organic mental disorders with depression: results of a double-blind multicenter study. *Aging (Milano).* 1993 Feb;5(1):63-71. doi: 10.1007/BF03324128. PMID: 8257478.
15. Sachdev PS, Parslow RA, Lux O, Salonikas C, Wen W, Naidoo D, Christensen H, Jorm AF. Relationship of homocysteine, folic acid and vitamin B12 with depression in a middle-aged community sample. *Psychol Med.* 2005 Apr;35(4):529-38. doi: 10.1017/S0033291704003721. PMID: 15856723.
16. Stahl SM. L-methylfolate: a vitamin for your monoamines. *J Clin Psychiatry.* 2008 Sep;69(9):1352-3. doi: 10.4088/jcp.v69n0901. PMID: 19193337.
17. Taylor MJ, Carney S, Geddes J, Goodwin G. Folate for depressive disorders. *Cochrane Database Syst Rev.* 2003;2003(2):CD003390. doi: 10.1002/14651858.CD003390. PMID: 12804463; PMCID: PMC6991158.

## Vitamin B12 (Methylcobalamin)

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 B12 in the form of methylcobalamin for Complete Methylation Support due to its enhanced ability to transport to tissues, which can be especially helpful in those with genetic transport B-12 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. Methylcobalamin has been studied in children with developmental delay and autism, and found to improve metabolic dysfunction as well as decrease autistic symptoms (3).

- 
1. Nashabat M, Maegawa G, Nissen PH, Nexo E, Al-Shamrani H, Al-Owain M, Alfadhel M. Long-term Outcome of 4 Patients With Transcobalamin Deficiency Caused by 2 Novel TCN2 Mutations. *J Pediatr Hematol Oncol*. 2017 Nov;39(8):e430-e436. doi: 10.1097/MPH.0000000000000857. PMID: 28538514.
  2. Office of Dietary Supplements, National Institutes of Health. Vitamin B-12 Fact Sheet for Health Professionals. Updated March 2022. Retrieved April, 12, 2022 at <https://ods.od.nih.gov/factsheets/VitaminB12-HealthProfessional/>
  3. Rossignol, D. A., & Frye, R. E. (2021). The Effectiveness of Cobalamin (B12) Treatment for Autism Spectrum Disorder: A Systematic Review and Meta-Analysis. *Journal of personalized medicine*, 11(8), 784. <https://doi.org/10.3390/jpm11080784>

## 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.

- 
1. Chen YS, Lee HF, Tsai CH, Hsu YY, Fang CJ, Chen CJ, Hung YH, Hu FW. Effect of Vitamin B2 supplementation on migraine prophylaxis: a systematic review and meta-analysis. *Nutr Neurosci*. 2021 Mar 29:1-12. doi: 10.1080/1028415X.2021.1904542. Epub ahead of print. PMID: 33779525.



2. Office of Dietary Supplements, National Institutes of Health. Riboflavin; Fact Sheet for Health Professionals. Updated May 2022. Retrieved May 16, 2022 at <https://ods.od.nih.gov/factsheets/Riboflavin-HealthProfessional/>
3. Sophia D. Amenyah, Amy McMahon, Mary Ward, Jennifer Deane, Helene McNulty, Catherine F. Hughes, J.J. Strain, Geraldine Horigan, John Purvis, Colum P. Walsh, Diane J. Lees-Murdock, Riboflavin supplementation alters global and gene-specific DNA methylation in adults with the MTHFR 677 TT genotype, *Biochimie*, Volume 173, 2020, Pages 17-26, ISSN 0300-9084, <https://doi.org/10.1016/j.biochi.2020.04.007>.

## Vitamin B6 (Pyridoxal 5-Phosphate)

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).

- 
1. Calderón-Ospina, C. A., & Nava-Mesa, M. O. (2020). B Vitamins in the nervous system: Current knowledge of the biochemical modes of action and synergies of thiamine, pyridoxine, and cobalamin. *CNS neuroscience & therapeutics*, 26(1), 5–13. <https://doi.org/10.1111/cns.13207>
  2. Hazra A, Kraft P, Lazarus R, et al. Genome-wide significant predictors of metabolites in the one-carbon metabolism pathway. *Hum Mol Genet.* 2009;18(23):4677-4687. doi:10.1093/hmg/ddp428
  3. McKinley MC, McNulty H, McPartlin J, et al. Low-dose vitamin B-6 effectively lowers fasting plasma homocysteine in healthy elderly persons who are folate and riboflavin replete. *Am J Clin Nutr* 2001;73:759-64
  4. Office of Dietary Supplements, National Institutes of Health. Riboflavin; Fact Sheet for Health Professionals. Updated March 2021. Retrieved May 16, 2022 <https://ods.od.nih.gov/factsheets/VitaminB6-HealthProfessional/>
  5. Parra, M., Stahl, S., & Hellmann, H. (2018). Vitamin B6 and Its Role in Cell Metabolism and Physiology. *Cells*, 7(7), 84. <https://doi.org/10.3390/cells7070084>

6. Tanaka T, Scheet P, Giusti B, et al. Genome-wide Association Study of Vitamin B6, Vitamin B12, Folate, and Homocysteine Blood Concentrations. *Am J Hum Genet.* 2009;84(4):477-482. doi:10.1016/j.ajhg.2009.02.011