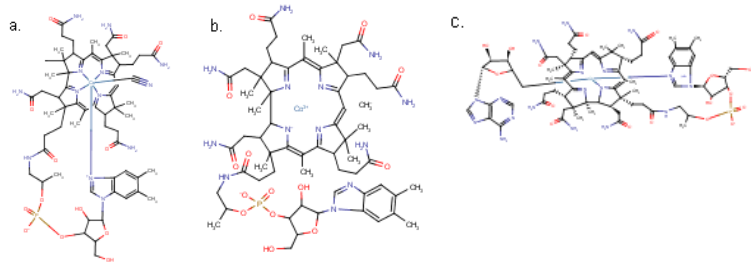


LIQUID B-12 5,000 mcg

TECHNICAL SUMMARY

Liquid B-12 is a complete B-complex formula that is high in vitamin B-12. B vitamins are often found together because, although each works independently of the others, they often function together in common metabolic pathways.* For example, most of the B vitamins are involved in energy production pathways.* In addition, vitamin B-12 and folic acid are both essential for the synthesis of DNA during cell division and therefore are important for rapidly multiplying cells, such as blood cells.* This formula contains 5,000 mcg of B-12 in three different forms to optimize its utilization.

Biochemistry: Liquid B-12 offers a balanced combination of B vitamins. It includes three forms of vitamin B-12: cyanocobalamin (5,6-dimethylbenzimidazolyl cyanocobamide)^a, methylcobalamin^b, and dibenzocide (Co α -[α -(5,6-dimethylbenzimidazolyl)]-Co β -(5'-deoxy-5'-adenosyl) cobamide)^c. Methylcobalamin and dibenzocide are present in their activated co-enzyme forms.



Molecular Formulas:

- Cyanocobalamin: C₆₃-H₈₈-Co-N₁₄-O₁₄-P
- Methylcobalamin: C₆₃-H₉₁-Co-N₁₃-O₁₄-P
- Dibenzocide: C₇₂-H₁₀₀-Co-N₁₈-O₁₇-P

Allergen and Additive Disclosure:

Not manufactured with wheat, gluten, soy, milk, egg, fish, shellfish or sesame ingredients. Produced in a GMP facility that processes other ingredients containing these allergens.

Delivery Form: Liquid.

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.*

Vitamin B-12 has two active forms, methylcobalamin (MeCbl) and adenosylcobalamin (AdCbl), each having distinct bodily functions.*

MeCbl is a cofactor of methionine synthase, an enzyme responsible for the production of methionine from homocysteine.* In vitamin B-12 deficiency, decreased MeCbl leads to the 'folate trap', a functional deficiency of folate.* This notably affects the rapidly dividing cells of the bone marrow.* U.S. data from the early 2000s show that B-12 depletion (148–221 pmol/L in serum) affects more than 20% of the population over the age of 60 and

Supplement Facts

Serving Size 1 Teaspoon (5 mL)
 Servings Per Container about 24

	Amount Per Serving	% Daily Value
Calories	10	
Total Carbohydrate	3 g	1%**
Thiamin (Vitamin B-1) (from Thiamin HCl)	3 mg	250%
Riboflavin (Vitamin B-2)	3.4 mg	262%
Niacin (Vitamin B-3) (as Niacinamide)	50 mg	313%
Vitamin B-6 (from Pyridoxine HCl)	10 mg	588%
Folate	1,360 mcg DFE (800 mcg folic acid)	340%
Vitamin B-12	5 mg (5,000 mcg)	208,333%
[as Cyanocobalamin, Methylcobalamin (Co-enzyme Form) and Dibenzocide (Co-enzyme Form)]		
Biotin	300 mcg	1000%
Pantothenic Acid (Vitamin B-5) (from Calcium Pantothenate)	50 mg	1000%

** Percent Daily Values are based on a 2,000 calorie diet.

Other ingredients: De-ionized Water, Vegetable Glycerin, Xylitol, L-Malic Acid, Natural Flavors, Organic Stevia Leaf Extract (Enzyme-Modified Steviol Glycosides), Potassium Sorbate (as preservative), Grapefruit Fiber and Cinnamon Bark Oil.

- 3 Forms of B-12 for Maximum Utilization
- Complete Liquid B-Complex

SUGGESTED USAGE: Shake well before use. In the morning, take 1 teaspoon, hold in mouth for 30 seconds, then swallow, or use as directed by your healthcare practitioner. Take with a meal. 1 teaspoon (5 mL) is equivalent to about 5 half dropperfuls.

14-16% of adults (20-59 y.o.). B-12 deficiency (<148 pmol/L in serum) affects up to 4% of adults (20-59 y.o.), and around 6% of persons aged 70 years and older. The prevalence of folate deficiency in the U.S. population is estimated at 0.5%.

AdCbl is the cofactor of methylmalonyl-CoA mutase, the enzyme that catalyzes the isomerization of methylmalonyl-CoA to succinyl-CoA, which is a key component of carbohydrate metabolism.* In vitamin B12 deficiency, decreased AdCbl leads to a decrease in this enzymatic reaction leading to anomalies of carbohydrate, fat, amino acid and urea metabolism, and affects the synthesis of neuronal myelin.*

Both MeCbl and AdCbl play important roles in the normal development and functioning of the central nervous system.*

Other B vitamins function as cofactors in key metabolic processes and can be summarized as follows:

- Thiamin: citric acid cycle*
- Riboflavin: cellular respiratory chain, energy metabolism, metabolism of neurotransmitters*

- Niacin: production of NAD/NADP*
- Vitamin B-6 (B-6): cellular energy production, glutathione and nucleotides biosynthesis, homocysteine recycling*
- Folate: biosynthesis of nucleotides and S-adenosylmethionine*
- Biotin: glucose and fat metabolism*
- Pantothenic acid: coenzyme A formation, fatty acid oxidation and other enzymatic reactions*
- Choline: biosynthesis of S-adenosylmethionine*
- Inositol (non-essential member of the vitamin B complex family): neurotransmitter signaling in the brain and central nervous system.*

NATUROKINETICS®

Liberation: Not applicable. Ingredients are in the form of a solution.

Absorption: The liquid form of this product is meant to maximize absorption. (Figure 1)

There are two known mechanisms for vitamin B-12 absorption: one that is complex and limited because it is Intrinsic Factor (IF)-dependent; and the other, by passive diffusion, which is virtually unlimited. After a single oral administration of vitamin B-12, no more than 3 µg can be absorbed through the IF-dependent mechanism. It occurs in the distal portion of the small intestine and requires IF, which is produced in the stomach, as well as by a properly functioning pancreas. The amount of vitamin B-12 absorbed via passive diffusion is about 1% of the orally administered dose and occurs throughout the length of the intestine.

Other B vitamins are absorbed in various parts of the intestine via several different mechanisms.

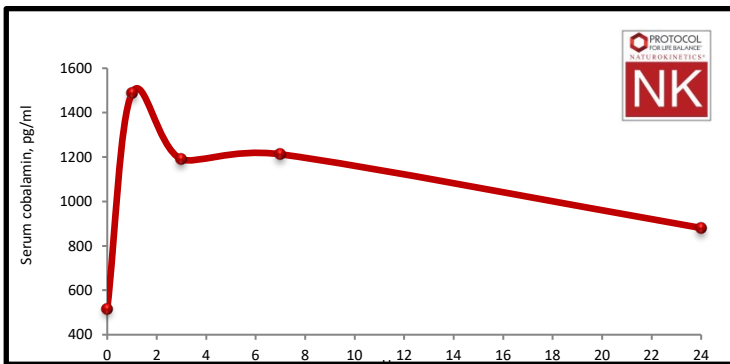


Figure 1: Average serum cobalamin level over a 24-hour period following the administration of a single dose of 10,000 mcg liquid B-12 (NOW Foods®, Bloomingdale, IL)

Distribution:

Absorbed cobalamin gets bound to specific binding proteins (transcobalamins, haptocorrins) and is transported to various tissues. It is then stored in the liver or kidneys, which maintain much of the approximately 2,500 µg of cobalamin in the body. At the cellular level, MeCbl is the predominant form existing in the cytoplasm and dibenzocozide is preferentially absorbed by mitochondria.

B-12 is also present in red blood cells, muscle, bones and the brain.

Other B vitamins' distribution in the body varies depending on the vitamin:

- Thiamin, with limited body storage, is mainly found in muscle tissues including the heart, liver, kidneys and brain.

- Riboflavin, with limited body storage, is found in most tissues with greater amounts found in the liver, heart and kidneys and, to a lesser extent, in the blood.
- B-6 is mainly stored in muscle tissue, and to a lesser extent in the liver.
- Folate, with limited body storage, is mainly found in the liver.
- Biotin accumulates in the liver; it is also found in significant amounts in the central nervous system and white blood cells.
- Pantothenic acid (B-5) is found throughout the body, where it is used for the synthesis of coenzyme A.*

Metabolism: In cells, B-12 is extensively metabolized through its co-enzymatic functions; metabolism of other B vitamins is complex and follows different pathways:

- Thiamin, once it reaches cells, is rapidly phosphorylated to form thiamin diphosphate (TPP). It can then be metabolized into thiamin monophosphate (TMP), and finally can be recycled back into thiamin.
- Riboflavin is metabolized to flavin mononucleotide, which can be used to form some flavoproteins, but it is mainly converted to flavin adenine dinucleotide (FAD), the predominant flavocoenzyme in body tissues.
- B-6 comprises a group of six related compounds: pyridoxal (PL), pyridoxine (PN), pyridoxamine (PM), and their respective 5'-phosphates [PLP (also known as P-5-P), PNP, and PMP]. Most of the absorbed B-6 is phosphorylated in the liver to form PNP, PLP, and PMP by PL kinase. PNP and PMP are then 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 via urine.
- Folate metabolism is complex and requires other B vitamins such as vitamins B-6, B-12 and NADP (a niacin derivative).
- Biotin is metabolized via *beta*-oxidation and sulfur oxidation.
- B-5 is metabolized in the liver to form coenzyme A, which is known for its role in the synthesis and oxidation of fatty acids, and the oxidation of pyruvate in the TCA cycle.*

Elimination: Absorbed cobalamin is excreted via the urine and the unabsorbed portion is excreted in feces. An estimated 1.4 µg/day of cobalamin is cleared and excreted into the bile, 70 % to 90 % of which is normally reabsorbed. The remaining portion is lost in the in feces. The daily amount of vitamin B-12 excreted from the body represents 0.1-0.2% of total body stores.

Other B vitamins are predominantly eliminated via urine. Biotin and riboflavin are also partially eliminated through the bile. Most of the folate excreted in the kidneys is reabsorbed in the proximal renal tubule.

CLINICAL VALIDATION

- In a double-blind, randomized, placebo-controlled clinical trial with 271 volunteers (aged ≥70 years), daily supplementation with a combination of B vitamins (5,000 mcg B-12, 800 mcg folic acid, 20 mg B-6 daily for 2 years) resulted in significant support of the markers of healthy brain tissue metabolism already within the normal range (as demonstrated by MRI screening), as compared to the placebo group.*

- In a double-blind, randomized, placebo-controlled clinical trial with 50 volunteers, supplementation with a combination of B vitamins (5,000 mcg B-12, 2,500 mcg folic acid, 25 mg B-6) for one year resulted in significant support of cardiovascular health (Figure 2) and healthy homocysteine levels.* (Figure 3)

SAFETY INFORMATION

Tolerability: This product has a long track record of excellent tolerability and safe use with nearly a million bottles sold since 2006.

However, B-vitamin supplementation could unmask the symptoms of polycythemia vera (a rare blood condition affecting 22 of every 100,000 individuals in the United States).

Contraindications: None known.

INTERACTIONS

Drug interactions, supplement interactions and interactions with lab tests have not been clinically evaluated for this specific blend of ingredients. However, medications such as some of those used to treat neuropsychiatric conditions, oral contraceptives, anticoagulants, and some antibiotics are known to interact with some of the vitamins present in this product, typically by depleting their availability for the body's usage. Contains Xylitol, which is harmful to pets. This product contains Biotin which may interfere with some blood test results. For the list of affected tests see: <https://www.fda.gov/medical-devices/in-vitro-diagnostics/biotin-interference-troponin-lab-tests-assays-subject-biotin-interference>

STORAGE

Refrigerate after opening to maximize freshness.

Quality studies performed in our state-of-the-art laboratories confirm the stability of Liquid B-12 5,000 mcg in real-time stability studies for at least 24 months.

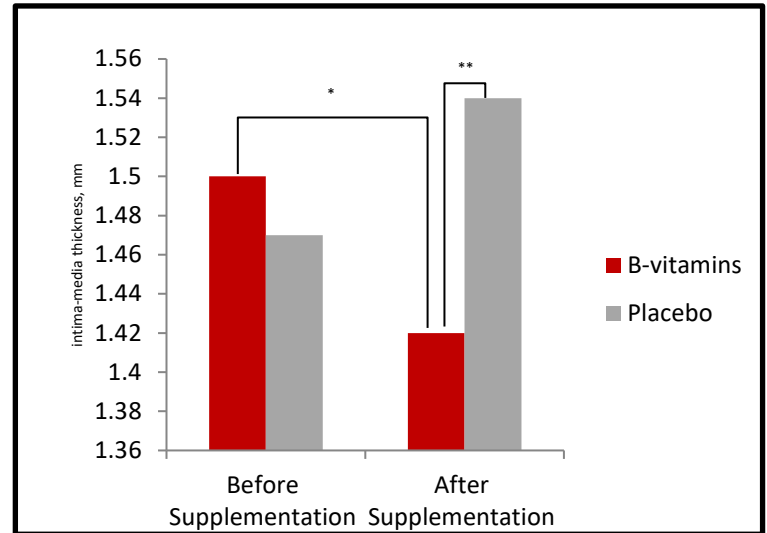


Figure 2: Evolution of intima-media thickness after one year supplementation with B-vitamins or placebo. *p=0.034 vs. baseline. **p=0.019 vs. placebo

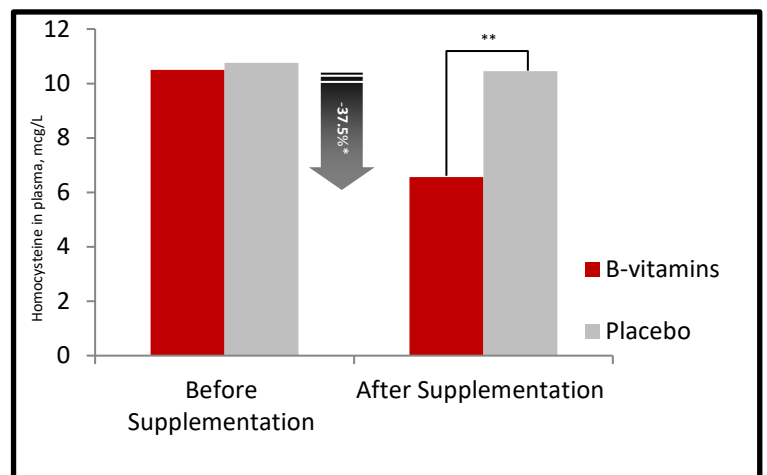


Figure 3: Evolution of homocysteine concentration in plasma after one year supplementation with B-vitamins or placebo. *p<0.001 vs. baseline. **p<0.001 vs. placebo