

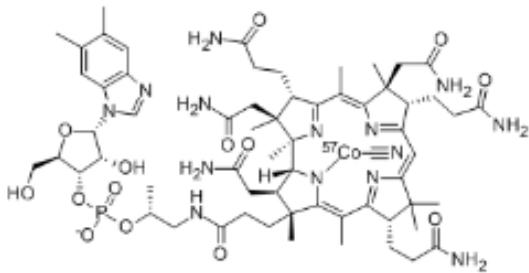
Nutri-Dose™ B-12 10,000 mcg

TECHNICAL SUMMARY

B vitamins are essential components in most major metabolic reactions as they play an important role in energy production, including the metabolism of lipids, carbohydrates, and proteins.* Vitamin B-12 facilitates energy production and is required for nucleic acid (DNA) synthesis, methionine synthesis from cysteine, and normal myelin synthesis in the nervous system.* Along with vitamin B-6, adequate levels of vitamin B-12 are required to maintain healthy plasma homocysteine levels.*

The elderly and strict vegetarians are often at risk for vitamin B-12 deficiency, either due to low dietary intake or decreased absorption. Nutri-Dose™ B-12 10,000 mcg is a convenient and palatable liquid formulation that is absorbed quickly by the body, delivering energizing nutrition.*

Structure Formula:



Chemical Name: 5,6-dimethyl-benzimidazolyl cyanocobamide

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 folate deficiency.* 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 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%.

Supplement Facts

Serving Size 1 Packet (15 mL) Servings Per Container 12

	Amount Per Serving	% Daily Value
Calories	25	
Total Carbohydrate	9 g	3%**
Total Sugars	0 g	†
includes 0 g Added Sugars		0%**
Sugar Alcohols (Xylitol & Erythritol)	4 g	†
Thiamin (Vitamin B-1) (from Thiamin HCl)	3 mg	250%
Riboflavin (Vitamin B-2) (from Riboflavin-5-Phosphate Sodium)	3.4 mg	262%
Niacin (Vitamin B-3) (as Niacinamide)	50 mg	313%
Vitamin B-6 (from Pyridoxine HCl)	10 mg	588%
Vitamin B-12 (as Cyanocobalamin)	10 mg (10,000 mcg)	416,667%
Biotin	300 mcg	1000%
Pantothenic Acid (from Calcium Pantothenate)	50 mg	1000%
Choline (from Choline Bitartrate)	5 mg	1%
Inositol	5 mg	†

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

† Daily Value not established.

Other ingredients: Water, Glycerin, Xylitol, Erythritol, Seven Berry Concentrate (Blueberry, Blackberry, Black Currant, Strawberry, Raspberry, Acai Berry, Cranberry), Natural Flavors, L-Malic Acid and Potassium Sorbate (as preservative).

- Convenient Vial Delivery System with Liquid B-Complex
- Mixed Berry Flavor

SUGGESTED USAGE: Shake before using. Tear off top at perforation and enjoy! Take one liquid packet daily with a meal, preferably in the morning, or as directed by your healthcare practitioner.

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 B-12 deficiency, decreased AdCbl leads to a decrease in this enzymatic reaction leading to anomalies of carbohydrate, fat, amino acid, and urea metabolism, and it also 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 nucleotide biosynthesis, homocysteine recycling*
- 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 of absorption for vitamin B-12: one complex, limited, and Intrinsic Factor (IF)-dependent, and one virtually unlimited via passive diffusion. 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 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.

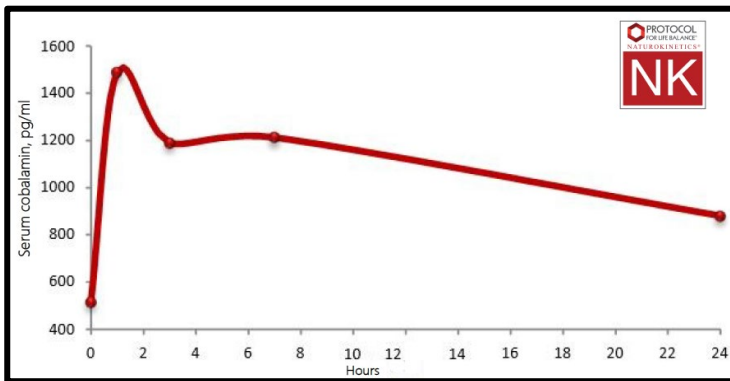


Figure 1: Average serum cobalamin level over a 24-hour period following the administration of a single dose of 10,000 mcg liquid B-12.

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 dibenzocoid is preferentially absorbed by mitochondria.

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

The distribution of other B vitamins 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.
- 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.
- 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 %¹⁵ 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 in 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.

STORAGE

Refrigerate after opening to maximize freshness.

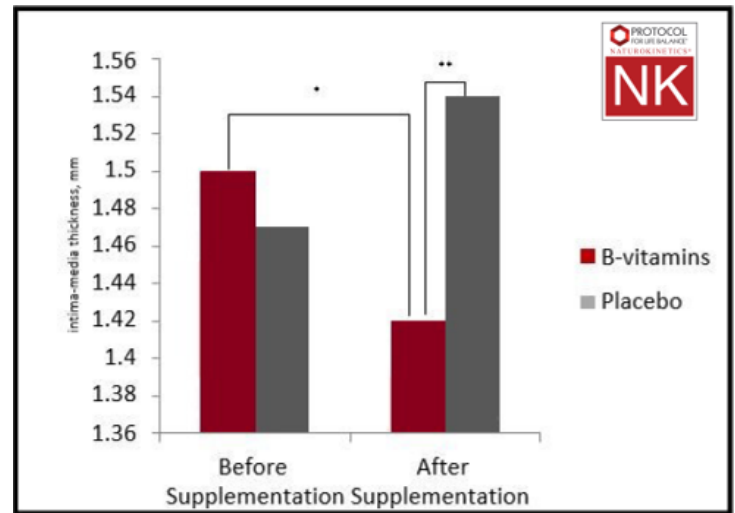


Figure 2: Evolution of intima-media thickness after one year supplementation with B-vitamins or placebo. *p=0.034 vs. baseline. **p=0.019 vs. placebo.

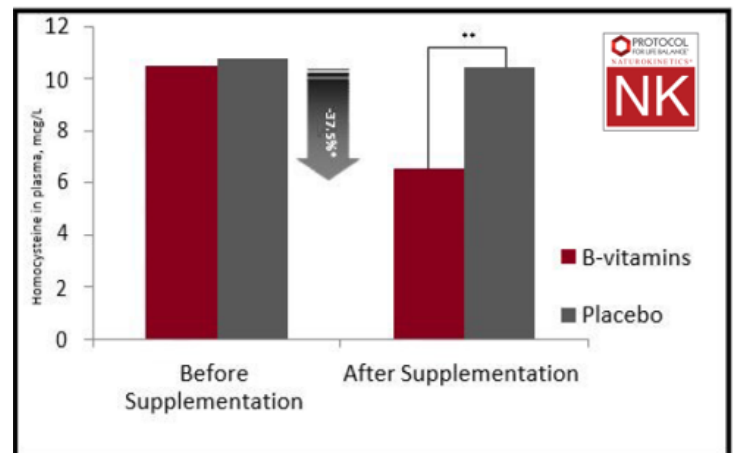


Figure 3: Evolution of homocysteine concentration in plasma after one year supplementation with B-vitamins or placebo. *p<0.001 vs. baseline. **p<0.001 vs. placebo.