

Vitamin B12

Summary of Benefits

Supports red blood cell production and reduces the risk of megaloblastic anemia (111).
Helps to prevent birth defects (112-114).
Supports bone health and reduces the risk of osteoporosis (115).
Improves mood (121).
Reduces the risk of macular degeneration (116).
Reduces brain atrophy, memory loss, and the risk of developing dementia (122-124).
Provides energy (125).
Lowers homocysteine levels (117-119).
Supports hair, skin, and nails (126).
(141).

Food sources

High amounts of vitamin B12 are found in foods like poultry, fish, eggs, and dairy.
Other foods high in vitamin b12 include
clams, fish, crab, low-fat roast beef, fortified soy milk, fortified cereal, fortified tofu, low-fat dairy, cheese (140).

Vitamin B12 occurs in three natural forms: methylcobalamin (MeCbl), adenosylcobalamin (AdCbl), and hydroxycobalamin (OHCbl). Cobalamins are compounds with vitamin B12 activity, which contain the mineral cobalt. The metabolically active forms of vitamin B12 are methylcobalamin and 5-deoxyadenosylcobalamin. Hydroxycobalamin and the synthetic form, cyanocobalamin, are other forms that become biologically active after conversion to methylcobalamin or 5-deoxyadenosylcobalamin.

Vitamin B12 is essential for the development, myelination, and function of the central nervous system, as well as for healthy red blood cell formation and DNA synthesis. Low vitamin B12 levels cause a reduction in red blood cell formation and prevent them from developing properly (111). Vitamin B12 acts as a cofactor for two enzymes: methionine synthase and L-methylmalonyl-CoA mutase. Methionine synthase converts homocysteine to methionine, which is necessary for the formation of S-adenosylmethionine (SAME), a methyl donor for various substrates including DNA, RNA, proteins, and lipids. SAME is arguably the best proven natural supplement for improving mood and symptoms of depression (some others include trimethylglycine, choline, vitamin D, adaptogens, and EPA). L-methylmalonyl-CoA mutase is involved in the metabolism of propionate, a short-chain fatty acid.

Adequate vitamin B12 levels are crucial to a healthy pregnancy. Studies show that a fetus's brain and nervous system require sufficient B12 levels from the mother in order to develop properly.

Vitamin B12 deficiency in the beginning stages of pregnancy may increase the risk of birth defects, such as neural tube defects. Furthermore, maternal vitamin B12 deficiency may contribute to premature birth or miscarriage (112-114).

Maintaining adequate vitamin B12 levels may support bone health. One study in 110 people with celiac disease found that low levels of vitamin B12 in males were linked to decreased bone mineral density in the femur and hips (115).

Macular degeneration is an eye disease that mainly affects your central vision (116). Maintaining adequate levels of vitamin B12 may help prevent the risk of age-related macular degeneration. Researchers believe that supplementing with vitamin B12 may lower levels of the amino acid homocysteine (117-119).

Elevated homocysteine levels have been associated with an increased risk of age-related macular degeneration (120). Vitamin B12 may improve your mood, albeit the effect of vitamin B12 on mood is not yet fully understood. Having said that, it plays a vital role in synthesizing and metabolizing serotonin, our "happy chemical" or "feel-good hormone" which plays an integral role in mood regulation (121).

Vitamin B12 deficiency has been associated with memory loss, especially in older adults (122,123), as it may play a role in preventing brain atrophy, which is the loss of neurons in the brain and often associated with memory loss or dementia (124).

Absorption, Measurement, and Deficiency

If you're significantly deficient in vitamin B12, taking a supplement or increasing your intake will likely improve your energy levels (125). Given vitamin B12's role in cell production, adequate levels of this vitamin are needed to promote healthy hair, skin, and nails (126).

In fact, low vitamin B12 levels can cause various dermatologic symptoms, including hyperpigmentation, nail discoloration, hair changes, vitiligo (patchy loss of skin pigmentation), and angular stomatitis (inflammation and cracking at the corners of the mouth) (127).

Regarding the digestive process, vitamin B12 is bound to protein in food and needs to be released prior to absorption. It commences in the mouth, where saliva mixes with food, freeing vitamin B12. Then it binds with haptocorrin, a cobalamin-binding protein in saliva. In the stomach, hydrochloric acid and gastric protease release more vitamin B12 from its food matrix, and it binds further to haptocorrin. In the duodenum, digestive enzymes release vitamin B12 from haptocorrin, and it combines with intrinsic factor, a binding protein secreted by parietal cells which originate in glands located in the fundus and body of the stomach. The resulting complex is absorbed in the distal ileum through receptor-mediated endocytosis. If vitamin B12 is already in free form, such as methylcobalamin, then it doesn't require the separation step.

The status of vitamin B12 in the body is typically assessed by measuring serum or plasma vitamin B12 levels. The cutoff for normal vitamin B12 levels versus deficiency varies depending on the method and laboratory, but subnormal values are generally defined as lower than 200 or 250 pg/mL (148 or 185 pmol/L). Serum methylmalonic acid (MMA) levels, a metabolite associated with vitamin B12, are the most sensitive markers of vitamin B12 status. An MMA level higher than 0.271 micromole/L suggests vitamin B12 deficiency. However, elevated MMA levels can also occur in the elderly and individuals with renal insufficiency. Another marker is total plasma homocysteine levels, which rise rapidly with declining vitamin B12 status. Serum homocysteine levels higher than 15 micromole/L suggests potential vitamin B12 deficiency. However, this marker has poor specificity as it can be influenced by other factors which affect homocysteine levels such as low consumption of riboflavin, folate, zinc, or TMG, and declining kidney function. Experts recommend that if a patient's serum vitamin B12 levels are less than 150 pg/mL (111 pmol/L), serum MMA levels should be checked to confirm a diagnosis of vitamin B12 deficiency.

Dosage Rationale

As aforementioned, there are three natural forms of vitamin B12 which are commercially available: methylcobalamin (MeCbl), adenosylcobalamin (AdCbl), and hydroxycobalamin (OHCbl). Albeit each of them has been shown to improve vitamin B12 status in clinical trials (143), methylcobalamin is the most bioavailable form (144), and is considered to retain better and for longer than the synthetic form cyanocobalamin (142). The RDA of vitamin B12 for adults is 2.4 mcg per day. Healthy subjects without deficiency typically absorb around a max of 10 mcg at a time, even at higher doses of up to 500 mcg (145). To be safe to meet the mark for maximal absorption and reduce the likelihood of deficiency while abstaining from an excessively high dose, we opted for 10 mcg of methylcobalamin in our Super U formula.

It's important to note that while these statements are based on available information in the scientific literature, it is always advisable to consult with a healthcare professional before making any changes to your supplementation or health routine.

RDA Intake Table:

According to the National Institutes of Health (NIH), the recommended daily intake for adult women is:

- B1: 1.1 milligrams (mg)
- B2: 1.1 mg
- B3: 14 mg NE
- B5: 5 mg
- B6: 1.3 mg
- Biotin: 30 micrograms (mcg)
- Folic acid: 400 mcg DFE
- B12: 2.4 mcg

For adult men, the NIH recommends the following daily intake:

- B1: 1.2 mg
- B2: 1.3 mg
- B3: 16 mg NE
- B5: 5 mg
- B6: 1.3 mg
- Biotin: 30 mcg
- Folic acid: 400 mcg DFE
- B12: 2.4 mcg (66)

REFERENCE

111. National Center for Biotechnology Information. (n.d.). <https://www.ncbi.nlm.nih.gov/books/NBK441923/>.

112. Wahbeh F, Manyama M. The role of Vitamin B12 and genetic risk factors in the etiology of neural tube defects: A systematic review. *Int J Dev Neurosci*. 2021 Aug;81(5):386-406. doi: 10.1002/jdn.10113. Epub 2021 Apr 22. PMID: 33851436.

113. Rogne, T., Tielemans, M. J., Chong, M. F.-F., Yajnik, C. S., Krishnaveni, G. V., Poston, L., Jaddoe, V. W. V., Steegers, E. A. P., Joshi, S., Chong, Y.-S., Godfrey, K. M., Yap, F., Yahyaoui, R., Thomas, T., Hay, G., Hogeveen, M., Demir, A., Saravanan, P., Skovlund, E., ... Risnes, K. R. (2017, February 1). Associations of maternal vitamin B12 concentration in pregnancy with the risks of preterm birth and low birth weight: A systematic review and meta-

analysis of individual participant data. American journal of epidemiology. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5390862/>.

114. Bala R, Verma R, Verma P, Singh V, Yadav N, Rajender S, Agrawal NR, Singh K. Hyperhomocysteinemia and low vitamin B12 are associated with the risk of early pregnancy loss: A clinical study and meta-analyses. *Nutr Res.* 2021 Jul;91:57-66. doi: 10.1016/j.nutres.2021.05.002. Epub 2021 May 24. PMID: 34134041.

115. Clarke M, Ward M, Dickey W, Hoey L, Molloy AM, Waldron L, Varghese A, McCann A, Blayney JK, McNulty H. B-vitamin status in relation to bone mineral density in treated celiac disease patients. *Scand J Gastroenterol.* 2015 Aug;50(8):975-84. doi: 10.3109/00365521.2015.1015603. Epub 2015 Apr 10. PMID: 25861707.

116. U.S. National Library of Medicine. (n.d.). PubMed. National Center for Biotechnology Information. <https://pubmed.ncbi.nlm.nih.gov/?SUBMIT=y>.

117. National Center for Biotechnology Information. (n.d.-a). <https://www.ncbi.nlm.nih.gov/books/NBK554408/>.

118. Nozari E, Ghavamzadeh S, Razazian N. The Effect of Vitamin B12 and Folic Acid Supplementation on Serum Homocysteine, Anemia Status and Quality of Life of Patients with Multiple Sclerosis. *Clin Nutr Res.* 2019 Jan 25;8(1):36-45. doi: 10.7762/cnr.2019.8.1.36. PMID: 30746346; PMCID: PMC6355946.

119. Kataria N, Yadav P, Kumar R, Kumar N, Singh M, Kant R, Kalyani V. Effect of Vitamin B6, B9, and B12 Supplementation on Homocysteine Level and Cardiovascular Outcomes in Stroke Patients: A Meta-Analysis of Randomized Controlled Trials. *Cureus.* 2021 May 11;13(5):e14958. doi: 10.7759/cureus.14958. PMID: 34123655; PMCID: PMC8191525.

120. Huang, P., Wang, F., Sah, B. K., Jiang, J., Ni, Z., Wang, J., & Sun, X. (2015, July 21). Homocysteine and the risk of age-related macular degeneration: A systematic review and meta-analysis. *Scientific reports.* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4508850/>.

121. Seppälä, J., Koponen, H., Kautiainen, H., Eriksson, J. G., Kampman, O., Leiviskä, J., Männistö, S., Mäntyselkä, P., Oksa, H., Ovaskainen, Y., Viikki, M., Vanhala, M., & Seppälä, J. (2013, May 24). Association between vitamin B12 levels and melancholic depressive symptoms: A Finnish population-based study. *BMC psychiatry.* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3674945/>.

122. Nalder L, Zheng B, Chiandet G, Middleton LT, de Jager CA. Vitamin B12 and Folate Status in Cognitively Healthy Older Adults and Associations with Cognitive Performance. *J Nutr Health Aging.* 2021;25(3):287-294. doi: 10.1007/s12603-020-1489-y. PMID: 33575718.

123. Issac, T. G., Soundarya, S., Christopher, R., & Chandra, S. R. (2015). Vitamin B12 deficiency: An important reversible co-morbidity in neuropsychiatric manifestations. *Indian journal of psychological medicine.* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4341306/>.

124. Gröber U, Kisters K, Schmidt J. Neuroenhancement with vitamin B12- underestimated neurological significance. *Nutrients.* 2013 Dec 12;5(12):5031-45. doi: 10.3390/nu5125031. PMID: 24352086; PMCID: PMC3875920.

125. Wolffenbuttel, B. H. R., Wouters, H. J. C. M., Heiner-Fokkema, M. R., & van der Klauw, M. M. (2019, May 27). The many faces of cobalamin (vitamin B12) deficiency. *Mayo Clinic proceedings. Innovations, quality & outcomes*.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6543499/>.

126. DiBaise M, Tarleton SM. Hair, Nails, and Skin: Differentiating Cutaneous Manifestations of Micronutrient Deficiency. *Nutr Clin Pract*. 2019 Aug;34(4):490-503. doi: 10.1002/ncp.10321. Epub 2019 May 29. PMID: 31144371.