

Vitamin B₁₂

Function

Vitamin B₁₂, the anti-pernicious anemia dietary factor, is the only known metabolite that contains cobalt. The various forms of vitamin B₁₂ are known collectively as cobalamins. In humans, vitamin B₁₂ is a cofactor in two enzymes that are fundamental in facilitating growth. In the methylcobalamin form, vitamin B₁₂ is the direct cofactor for methionine synthetase, the enzyme that recycles homocysteine back to methionine. Here, vitamin B₁₂ and folic acid have closely related roles in one-carbon metabolism. In the adenosylcobalamin form, vitamin B₁₂ is the cofactor in methylmalonyl-coenzyme A mutase. Both reactions are involved in promoting the rapid growth and proliferation of bone marrow cells.

Vitamin B₁₂ is also essential for the function and maintenance of the central nervous system, and severe deficiency in persons with pernicious anemia produces the neurological disease of posterolateral spinal cord degeneration (Herbert and Das 1999). The direct cause of pernicious anemia, in fact, is vitamin B₁₂ deficiency, but the underlying defect is the absence of an intrinsic factor produced by specific stomach cells and needed for intestinal absorption of vitamin B₁₂. Without this intrinsic factor absorption fails and a severe and persistent deficiency develops that is not prevented by the usual dietary levels of vitamin B₁₂. In addition to the efficient, intrinsic factor-mediated absorption of small quantities of the vitamin from normal dietary intakes of up to about 6 µg, there is also a very low efficiency of absorption of much higher oral intakes (300 to 1,000 µg). Therefore, high daily oral intakes can be sufficient to treat pernicious anemia, although the usual treatment is a monthly injection (Hathcock and Troendle 1991).

Safety Evidence

No toxic effects of B₁₂ have been encountered in humans or animals at any level of oral intake (Miller and Hayes 1982; Food and Nutrition Board 1998). The overall evidence indicates that vitamin B₁₂ is virtually nontoxic. Doses of 1,000 µg per day were administered to a child by intravenous injection for a year without adverse effect (Merck 1958). Even if 100 percent metabolic liberation from cyanocobalamin is assumed, the cobalt and cyanide contributions of 1,000 µg of vitamin B₁₂ are toxicologically insignificant (Hathcock and Troendle 1991).

One case of cobalamin-induced acne has been reported in association with an unspecified dosage administered by injection twice a week (Dupre et al. 1979), and a single case of contact dermatitis has also been reported (Rodriguez et al. 1994).

Published Official Reviews of Vitamin B₁₂ Safety

The FNB concluded that “no adverse effects have been associated with excess B₁₂ intake from food or supplements in healthy individuals” (Food and Nutrition Board 1998). Consequently, FNB concluded that there was no basis for a UL value.

Likewise, EC SCF reviewed vitamin B₁₂ and, concluding that there were no adverse effects known for vitamin B₁₂, found no basis for deriving a UL value (Scientific Committee on Food 2000).

The UK EVM found no evidence of adverse effects of vitamin B₁₂ in humans (Expert Group on Vitamins and Minerals 2003), but stated that subcutaneous or intraperitoneal injections of 1.5 to 3 mg per kg body weight were acutely toxic to mice (Tsao and Myashita 1993). The report concluded that there was no basis for an SUL for oral vitamin B₁₂, but set a GL of 2,000 µg based on a clinical trial (Juhlin and Olsson 1997) as well as other data showing no adverse effects.

CRN ULS (OSL Method) for Vitamin B₁₂

The FNB’s observation of a lack of any adverse effects for vitamin B₁₂, combined with the extensive testing and use of oral vitamin B₁₂ dosages of up to 1,000 µg in pernicious anemia patients (Hathcock and Troendle 1991), would suggest that high dosages of vitamin B₁₂ are safe for such persons.

Vitamin B₁₂ has no observable adverse effect at any level of oral intake, even when consumed parenterally at 1,000 µg (1 mg) twice weekly for up to three years, or intravenously at 1 mg per day for one year. Thus, there is no basis for a LOAEL for oral intake.

There is considerable experience and clinical evidence of safety at oral intakes of 3,000 µg (3 mg) per day, and higher intakes may also be safe. Thus, the CRN OSL is set at 3,000 µg of supplemental vitamin B₁₂ per day. Dietary intake is trivial in comparison with this amount of supplement.

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<u>Comparison of Safety Values for Vitamin B₁₂</u>	
CRN ULS (OSL method)	3,000 µg
US FNB UL	Reviewed but not established (no toxicological basis)
EC SCF UL	Reviewed but not established (no toxicological basis)
EC supplement maximum	Not established (as of May 2004)
UK EVM GL	2,000 µg

References

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