# Cyanocobalamin vs. Methylcobalamin

#### Three misleading information to be clarified:

- 1. Cyanocobalamin is toxic.
- 2. Methylcobalamin is natural.
- 3. People with methylation problem should take methylcobalamin since supplemental methylcobalamin is the ready-to-work coenzyme (cofactor) form.



# 1. Cyanocobalamin is safe, NOT toxic!

- If you eat ONLY 1 g of almond (1 whole piece), you can ingest 15.6 times higher cyanide than taking 1 serving of cyanocobalamin from Shaklee B complex. 1-3
- Most clinical studies used cyanocobalamin, NOT methylcobalamin, to solve vitamin B<sub>12</sub> deficiencies, without showing any toxic effects
- CDC indicated following in the section on "How can cyanide affect my health?"
  - $\triangleright$  "Vitamin B<sub>12</sub>, a natural chemical containing cyanide, is beneficial to your body because it prevents anemia. The cyanide binds in vitamin B<sub>12</sub> so that it does not serve as a source of cyanide exposure and cannot harm you."
- Since cyanocobalamin is NON-toxic, cyanide toxicity is treated by injecting hydroxocobalamin, so that cyanide can bind with the cobalamin to form non-toxic cyanocobalamin in the cell and then to be excreted via urine safely.<sup>5,6</sup>
  - 1. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3793392/pdf/ISRN.TOXICOLOGY2013-610648.pdf
  - 2. http://www.answers.com/Q/How many almonds are in 1 gram
  - 3. <a href="http://nordicfoodlab.org/blog/2013/8/hydrogen-cyanide">http://nordicfoodlab.org/blog/2013/8/hydrogen-cyanide</a>
  - 4. http://www.atsdr.cdc.gov/phs/phs.asp?id=70&tid=19
  - 5. http://epmonthly.com/article/hydroxocobalamin-turning-cyanide-into-vitamin-b12/
  - 6. https://www.health.ny.gov/environmental/emergency/chemical\_terrorism/cyanide\_tech.htm



#### Cyanide Concentrations in Foods

# Common foods contain much higher amount of cyanide than the supplement containing cyanocobalamin which includes 2% of cyanide. 1,2

			Cyanide content (mg/kg)	Average levels (mg/kg)	Standard error (mg/kg)
Sweet almond	Varieties	Variety1	27		
		Variety2	32.40	25.20	8.24
		Variety3	16.20		
Bitter almond	Origin	Sfax <sub>1</sub>	1053		
		Sfax <sub>2</sub>	1215	1062	148.70
		North	918		
Apricot kernels	Origin	Tastour	540		
		Sfax	583.20		
		Sbiba	804.60	851.04	303.28
		Monastir	1134		
		Morneg	1193.40		

Type of product	Cyanide concentration (in mg/kg or mg/L)		
Cereal grains and their products	0.001-0.45		
Soy protein products	0.07-0.3		
Soybean hulls	1.24		
Apple seeds	500-700		
Apricot pits, wet weight	89-2170		
Home-made cherry juice from pitted fruits	5.1		
Home-made cherry juice containing 100% crushed pits	23		
Commercial fruit juices			
Cherry	4.6		
Apricot	2.2		
Prune	1.9		
Tropical foodstuffs			
Cassava (bitter) - dried root cortex	2360		
Cassava (bitter) - whole tubers	380		
Cassava (sweet) - whole tubers	445		
Sorghum - whole immature plant	2400		
Bamboo - immature shoot tip	7700		
Lima beans from Java (coloured)	3000		
Lima beans from Puerto Rico (black)	2900		
Lima beans from Burma (white)	2000		

#### **EXPLANATIONS:**

- The molecular mass of cyanocobalamin is 1355.38 g/mol whereas that of cyanide is 26.02. Therefore, the percent of cyanide in cyanocobalamin is about 2% (26 / 1355 = 0.02; 0.02 x 100 = 2%).
- Shaklee B complex contains 1.6 mcg of cyanide from 81 mcg of cyanocobalamin.
- The average cyanide content in sweet almonds is 25.20 mg/kg as shown in the Table 1.
- It means there is 25 mcg of cyanide in 1 g of sweet almond (one piece of almond).
- So, there is 15.6 times higher cyanide in one almond than cyanocobalamin from Shaklee B complex (25/1.6=15.6).

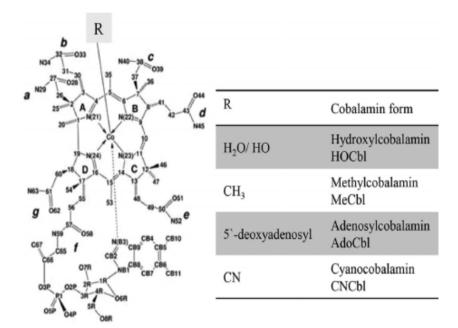
(NOTE: The weight of one almond is about 1 gram and bitter almonds contain a lot higher cyanide.)



- 1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3793392/pdf/ISRN.TOXICOLOGY2013-610648.pdf
- 2. http://nordicfoodlab.org/blog/2013/8/hydrogen-cyanide

#### Several Forms of Cobalamin

- There are several cobalamin forms of vitamin B12 according to the ligand:
  - ✓ Cyanocobalamin (cyanide group)
  - ✓ Adenosylcobalamin (5'deoxyadenosyl group)
  - ✓ Hydrocobalamin (=aquacobalamin: H₂O)
  - ✓ Hydroxocobalamin (=hydroxycobalamin: OH)
  - ✓ Methylcobalamin (methyl group)





# Methylcobalamin that is used in dietary supplements can be produced by bacteria.



5'-deoxyadenosylcobalamin and methylcobalamin as sources for vitamin B<sub>12</sub>

#### Methylcobalamin

The petitioner indicates that methylcobalamin may be manufactured semi-synthetically following extraction of vitamin  $B_{12}$  from animal material. The petitioner states that alternatively, it may be produced from Genetically Modified Micro-organisms (GMMs).



#### What is the starting material for chemically synthesized methylcobalamin?

Cyanocobalamin or hydroxocobalamin

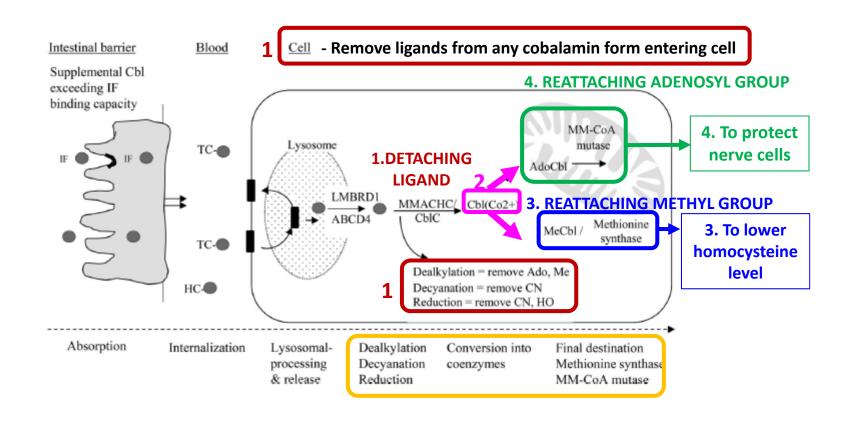
# Process for production of methylcobalamin US 6657057 B2

#### ABSTRACT

The present invention provides an industrially excellent and novel process for producing methylcobalamin useful as medicines. Namely, it provides a process for producing methylcobalamin, which comprises the step of methylating cvanocobalamin or hydroxocobalamin in the presence of a reducing agent and a water-soluble methylating agent.



#### **Cobalamin Processing in the Cell:**

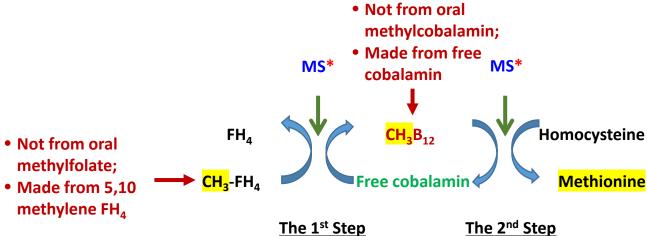


- 1. Ligand removal (all ligand to be removed via dealkylation, decyanation, or reduction)
- 2. Form a free form of cobalamin (Cbl)
- 3. Reattaching methyl group to be make "methylcobalamin," a cofactor for methionine synthase
- 4. Reattaching adenosyl group to make "adenosylcobalamin," a cofactor fro Methylmalonyl CoA Mutase



# Methylcobalamin

#### Re-methylation (the 1st step) and De-methylation (the 2nd step) of Cobalamin



The 1st Step: transferring methyl (-CH<sub>3</sub>) group from CH<sub>3</sub>-FH<sub>4</sub> to free cobalamin to re-synthesize CH<sub>3</sub>B<sub>12</sub> (methylcobalamin)

- **FH**<sub>4</sub>: Tetra-hydro-folate
- CH<sub>3</sub>-FH<sub>4</sub>: Tetra-hydro-methyl-folate (THMF)

The 2<sup>nd</sup> Step

The 2<sup>nd</sup> Step: transferring methyl (-CH<sub>3</sub>) group from methylcobalamin (CH<sub>3</sub>B<sub>12</sub>) to Homocysteine to synthesize Methionine, re-generating free-B<sub>12</sub>

- CH<sub>3</sub>B<sub>12</sub>: Methylcobalamin
- Co(I, or II)B<sub>12</sub>: Free-cobalamin

\*MS: Methionine Synthase = homocysteine: methionine methyltransferase



### Truth about Methylcobalamin

- Oral methylcobalamin does <u>NOT</u> reach the destination as the ready-towork form because the cofactor form of methylcobalamin has to be resynthesized (REMETHYLATED) in the cell from the free cobalamin.
- "Supplementing methylcobalamin (or adenosylcobalamin) is unlikely to be advantageous when compared to cyanocobalamin" because:
  - ✓ methylcobalamin (or adenosylcobalamin) follows the same route of intracellular processing as cyanocobalamin and
  - ✓ methylcobalamin can be derived from cyanocobalamin



## **CONCLUSION** on Vitamin B12

- 1. Cyanocobalamin is Safe and the most studied form of B12 (24,475 articles in PubMed).
- 2. Methylcobalamin is likely produced by bacteria or derived from cyanocobalamin.
- 3. NO difference between cyanocobalamin and methylcobalamin to function in the body:
  - Supplemental methylcobalamin is NOT the ready-to-use coenzyme form
  - <u>People with methylation defect can utilize cyanocobalamin</u> since cyanocobalamin can be efficiently converted to methyl- or adenosyl-cobalamin.
- 4. Would it help to take methylcobalamin over cyanocobalamin when told you have a "methylation defect"? → NO
- 5. There are a lot more cyanide from natural food sources than the cyanide from cyanocobalamin in Shaklee supplements per serving.
- 6. To detoxify cyanide poisoning, hydroxocobalamin is injected (i.v.) to form cyanocobalamin in the body because:
  - making cyanocobalamin is a way to remove cyanide from the body safely
  - cyanocobalamin is non-toxic and excreted via urine safely



#### **Reference for Vitamin B12**

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