

Fortify Your Life



Tieraona Low Dog, MD

Chair: US Pharmacopeia
Dietary Supplements Admissions Joint
Standard Setting Sub-Committee

Author of National Geographic's "Fortify
Your Life" and
"Healthy At Home" and
"Life Is Your Best Medicine"

www.DrLowDog.com

Tieraona Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC.
All Rights Reserved.

Food is Foundational



Tieraona Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC.
All Rights Reserved.



Tieraona Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC.
All Rights Reserved.

The State of American Nutrition

- Typical American diets exceed recommended intake levels in four categories: calories from solid fats and added sugars; refined grains; sodium; and saturated fats.
- CDC results indicate that <18% of adults in each state consumed the recommended amount of fruit and <14% consumed the recommended amount of vegetables.

www.cdc.gov/nmmwr/preview/mmwrhtml/mm6426a1.htm Accessed December 20, 2016

Tieraona Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC.
All Rights Reserved.

Food Quality

- Agricultural methods have increasingly stripped amounts of nutrients from the soil. Nutrient deficient soil yields nutrient deficient food.
- We may be seeing a genetic dilution with high-yield varieties with more carbohydrate but fewer nutrients. Increasing use of pesticides may also decrease plant secondary metabolites.
- Studies in wheat show 50% decline in protein, and in produce, we have seen a 22-29% decline in 6 minerals over the past 100 years; broccoli has roughly 1/3 the calcium it did in 1950.

Davis, DR. Declining fruit and vegetable nutrient composition: What is the Evidence? *HortScience* 2009; 44:15-19.

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC
All Rights Reserved.

Do You Believe?

- Most Americans get all the micronutrients they need in their diet.
- Nutrient deficiencies are rare in the United States.
- That dental and medical communities are adequately trained to recognize nutrient deficiencies in their clinical practice.

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC
All Rights Reserved.

Real State of Our Nutrition

- 90 million Americans are vitamin D deficient (using the Endocrine Society guidelines < 20ng/mL)
- 30 million are deficient in vitamin B6
- 18 million people have B12 deficiency
- ~16 million have very low serum vitamin C
- 13% of Latinas and 16% of African American women (ages 12-49) are iron deficient
- Women 25-39 overall have borderline iodine insufficiency



CDC: 2nd National Report on the Biochemical Indicators of Diet and Nutrition in the U.S. population

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC
All Rights Reserved.

Case 41-year old Female

- Strict vegan for 2.5 years. Disturbance of taste (unable to sense flavor of variety of fruits and vegetables), fatigue after simple daily activities, paresthesia of the anatomic structures innervated by the mandibular division of the trigeminal nerve on her left side, disturbance of memory and slowing mental faculty. No meds. No significant medical or dental history.

Pontes HA, et al. *J Can Dent Assoc* 2009; 75(7):533-7.

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC
All Rights Reserved.



Figure 1a: Papillary atrophy and erythema involving the lateral border of the tongue before treatment.

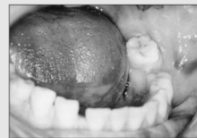


Figure 1b: Erythema involving the mucosa of the cheek and the anterior portion of the tongue.



Figure 1c: Well-circumscribed erythematous macules seen on the lateral border of the tongue.



Figure 1d: Erythema involving the mucosa of the right cheek.

Vicanna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Laboratory Tests

Test	Normal range (female)	Patient's values
RBC count (cells/ μ L)	3.90–5.03	1.63
Hemoglobin (g/dL)	12.0–15.5	7.2
MCV (fL)	80–100	144
Hematocrit (%)	36–45	23.4
RDW (%)	13 \pm 1.5	25
Serum folate (ng/mL)	3–16	7.73
Serum cobalamin (pmol/L)	118–716	71.8

MCV = mean corpuscular volume; RBC = red blood cell; RDW = red cell distribution width.

Vicanna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.



Figure 2a: Dramatic resolution of erythema and all pathologic symptoms after 1 week of treatment with parenteral doses of cobalamin and folic acid.



Figure 2b: Absence of papillary atrophy and erythema previously seen on the lateral border of the tongue.



Figure 2c: Tissue regeneration on the mucosa of the cheek appeared complete after 2 weeks of treatment.

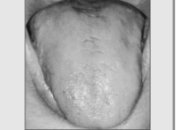


Figure 2d: Complete tissue regeneration on the tongue after treatment.

Patient treated with 1000 mcg B12 IM per week for 4 weeks and 1 mg folate daily. Symptoms disappeared after 14 days of treatment.

Vicanna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

B-Vitamins

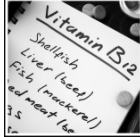
- The B-vitamins are important for the metabolism of carbohydrates, fats and proteins and play a vital role in the production of fuel and energy for the body.
- There are eight B-vitamins that partner together, which is why you almost always want to take them together in balanced amounts.



Vicanna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Vitamin B12



- Atrophic gastritis affects 10%-30% of people over 60 years of age causing malabsorption of food bound vitamin B12.
- Low vitamin B₁₂ concentrations can cause serious problem; **peripheral neuropathy, balance disturbances, cognitive disturbances, physical disability, and greater loss of bone density.**
- American Academy of Neurology recommends elders and anyone with suspected dementia, be checked for B12 deficiency.
- Risk: inadequate intake, veganism, malabsorption, medications (PPI, metformin), obesity, aging.
- **18 million Americans are frankly deficient** in vitamin B12.
- Supplement with 20-100 mcg per day.

Copyright © Medicine Lodge Ranch, LLC
All rights reserved.

Niafar M, et al. *Intern Emerg Med* 2015; 10(1):93-102.

Vicenna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC
All Rights Reserved.

Metformin With Proton Pump Inhibitors: A Polypharmacy Recipe for Neuropathy via Vitamin B12 Depletion

Zabala MJ. *Clin Diabetes* 2015; 33(2):90-5.



Meta analysis: 29 studies (8,089 patients) found **245% increased risk of B12 deficiency associated with metformin use.**

Niafar M, et al. *Intern Emerg Med* 2015; 10(1):93-102

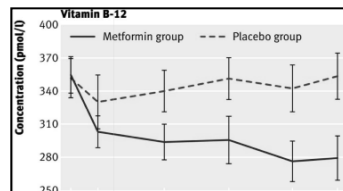
Vicenna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC
All Rights Reserved.

Metformin and Vitamin B-12

Study of 390 patients with type 2 diabetes randomized to metformin (850 mg) or placebo T1D for 4.3 years.

Compared with placebo, metformin treatment was associated with a mean decrease in vitamin B-12 concentration of -19%.

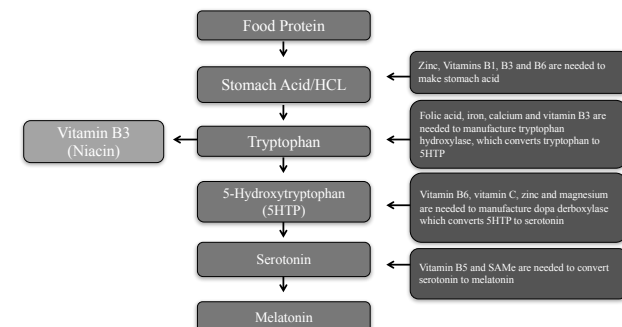


De Jager, et al. *BMJ* 2010; 340:c2181

Vicenna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC
All Rights Reserved.

Serotonin and Melatonin Pathways



Vicenna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC
All Rights Reserved.

Which of the following micronutrients is needed to convert vitamin B6 to the active form of pyridoxal 5 phosphate in the liver?

- A. Iron
- B. Zinc
- C. Riboflavin
- D. Vitamin A

Vicanna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

•The correct answer is C.

•**Riboflavin** is needed to convert all forms of **vitamin B6** to the active form of PLP. **Zinc** is needed by cells to take up PLP.

Vicanna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

65-year old man complains of persistent tingling and numbness in his legs (bilateral) during a routine oral care visit. Dentist notes he has a beefy red and deeply fissured tongue and complains of sore throat. Other than cataract in his right eye, no known medical problems. Vegetarian and lactose intolerant. Which of the following nutrient deficiencies would best explain his symptoms?

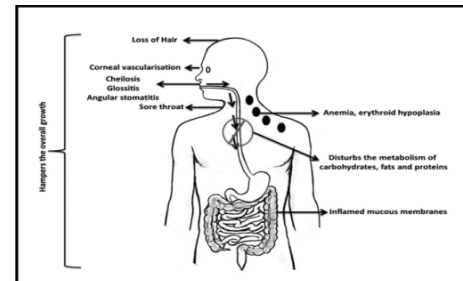
- A. Vitamin B2
- B. Vitamin B6
- C. Vitamin C
- D. Vitamin B12



From McLaren DS: *A colour atlas and text of diet-related disorders*, ed 2, London, 1992, Mosby-Year Book.

Vicanna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.



Riboflavin (B2) deficiency causes ariboflavinosis, which manifests as cracked lips, inflammation of the tongue, dryness or burning of the oral cavity, and sore throat.

Vicanna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

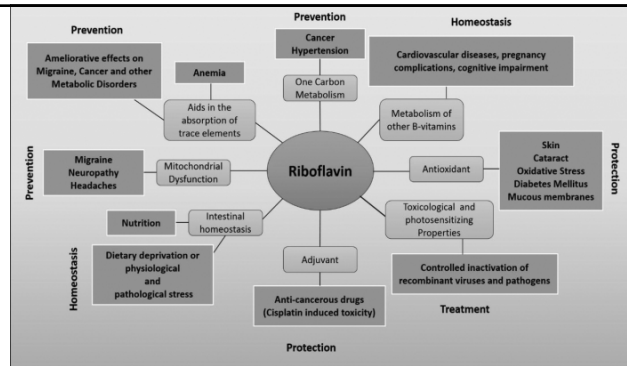


Fig. 6 Physiological functionality of Riboflavin

Published in: Kiran Thakur, Sudhir Kumar Tomar, Ashish Kumar Singh, Surajit Mandal, Sumit Arora, *Critical Reviews in Food Science and Nutrition* just-accepted, 08-08, DOI: 10.1080/10408398.2016.1145104 Copyright © 2016 Taylor & Francis Group, LLC.

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Riboflavin Deficiency: At Risk Groups

- Excessive alcohol intake
- Those with **chronic infection or liver disease** (increased demand)
- **Inflammatory bowel disease** (decreased absorption)
- **Diabetics** (increased excretion)
- **Elders** (decreased absorption, dietary intake)
- **Vegans** (insufficient dietary intake)
- **Pregnant and breastfeeding women** (increased demand – low riboflavin increases risk for pre-eclampsia)
- **Adolescents, particularly girls** (increased demand)
- **Athletes** (increased demand)
- **Hyperthyroidism** (increased demand)
- **MTHFR C667T** genotype (increased demand)
- Brown-Vialetto-Van Laere syndrome genetic neurological disorder mutation in transporter: deafness, bulbar palsy, respiratory difficulties)

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Choline: Related to B-Vitamins

- Choline deficiency causes **abnormal deposition of fat in the liver**, which results in **nonalcoholic fatty liver disease**.
- Necessary for healthy cell membranes and **cognition** as we age.
- Water soluble nutrient in the B-vitamin family that is particularly **crucial during pregnancy and first 3 years of a child's life**.
- New daily value set in 2016: **550 mg per day**

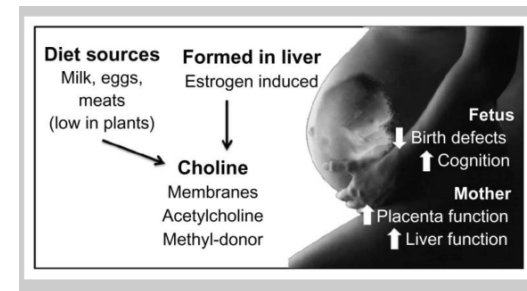
Jiang X, et al. *Trends Endocrinol Metab* 2014; 25(5):263-73.

Jiang X, et al. *FASEB J*. 2012;26(8):3563–3574.

Wozniak JR, et al. *Nutr Res* 2013; 33(11):897-904

Vianna Low Dog, M.D.

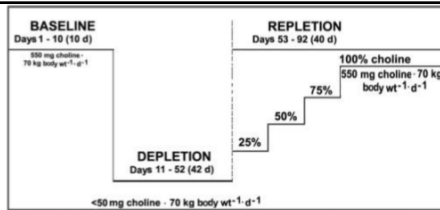
Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.



Zeisel SH. *Int J Womens Health*. 2013; 5: 193–199.

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.



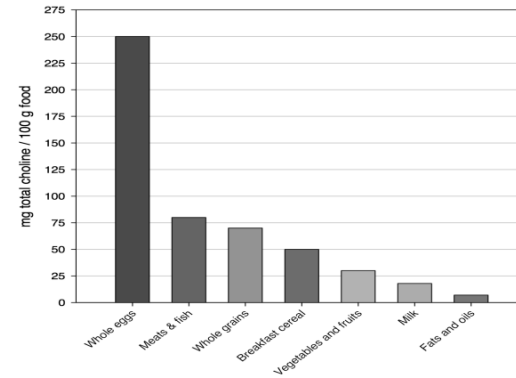
- 57 healthy adults were fed choline-deficient diets under controlled conditions.
- Results showed that 77% of men, 80% of postmenopausal women, and 44% of premenopausal women developed fatty liver, liver damage, and/or muscle damage.
- Dysfunction corrected when choline was reintroduced into diet.

Fischer LM, et al. *Am J Clin Nutr*. 2007;85(5):1275-1285.

Viviana Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Choline in Foods: <http://naldc.nal.usda.gov/download/47335/PDF>



Viviana Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Nutrient	Yolk	White	% Yolk	% White
Protein	2.7 g	3.6 g	43%	57%
Fat	4.5 g	0 g	100%	0%
Cholesterol	0.21 mg	0 mg	100%	0%
Sodium	0.008 mg	0.055 mg	13%	87%
Folate	24.8 mcg	1.3 mcg	95%	5%
Calcium	21.9 mg	2.3 mg	90%	10%
Magnesium	0.9 mg	3.6 mg	20%	80%
Potassium	18.5 mg	53.8 mg	26%	74%
Phosphorous	66.3 mg	4.9 mg	93%	7%
Selenium	9.5 mcg	6.6 mcg	59%	41%
Vitamin A	244 IU	0 IU	100%	0%
Vitamin E	0.5 mg	0 mg	100%	0%
Vitamin B12	0.6 mcg	0 mcg	100%	0%
Choline	126 mg	0.4 mg	100%	0%

Viviana Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.



Viviana Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

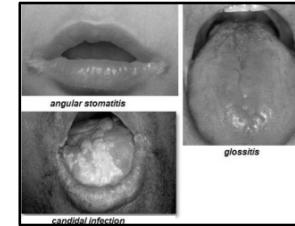
A 26-year old African American woman comes in for her routine dental exam. She mentions that she craves ice all the time, even in the winter. Dentist notes generalized oral mucosal atrophy and pallor. What nutrient deficiency is most likely?

- A. Folate
- B. Iron
- C. Calcium
- D. Selenium

Victoria Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

- Review of Systems May Yield
 - Shortness of breath
 - Fatigue
 - Sensitivity to cold
 - Muscular weakness
 - Low blood pressure
 - Restless legs
 - Pica (chew ice or non-food items)
- Physical Exam Findings
 - Angular cheilitis
 - Atrophic glossitis
 - Generalized oral mucosal atrophy
 - Candida infections
 - Mucosal pallor
 - Stomatitis
 - Nonspecific pallor of the mucous membranes



Correct answer is B: Iron

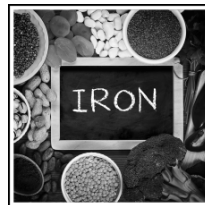
Victoria Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Iron

Most common nutrient deficiency in world, affecting 2 billion people.

- Iron deficiency anemia accounts for **20% of all global maternal deaths**.
- Necessary for growth and development and essential component of Hg.
- Iron promotes resistance to disease; improves health of the teeth, skin, and bones; maintains energy.
- Two forms of iron: **heme and non-heme**.
- Meat contains both forms, while plants and fortified foods contain only non-heme iron.
- **We absorb roughly 18% of iron present in meat, compared to about 10% in plants**



Victoria Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Pregnancy: Increased Need

- The American Academy of Family Physicians, U.S. Preventive Services Task Force, and Centers for Disease Control and Prevention recommend routine screening of pregnant women for low iron.
- During pregnancy, body needs higher levels of iron because of the growing fetus, higher volume of blood, and blood loss that will occur during delivery.
- If a pregnant woman does not get enough iron, her baby is at higher risk for **being born prematurely with a low birth weight, lower IQ and poorer neurocognitive development**.



Victoria Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Menstruation and Iron

- Marked differences between women in menstrual blood loss (10-250 mL per menses).
- Low iron levels are the most common cause of anemia in adolescent girls and can be very detrimental to mood and cognition, as well as physical well-being.
- Heavy menstrual bleeding is a significant risk for iron deficiency and is often overlooked.
- Data from cycle 2 (2009 to 2011) of Canadian Health Measures Survey, depleted iron stores were found in **13% of females aged 12-19** and **9% of females aged 20-49**.



Blitacz L, et al. *Gynecol Endocrinol* 2014;30(8):542-8.
Nelson AL, et al. *Am J Obstet Gynecol* 2015; 213(1):97.e1-6.
Cooper M, et al. *Health Rep* 2012;23(4):41-8.

Viviana Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

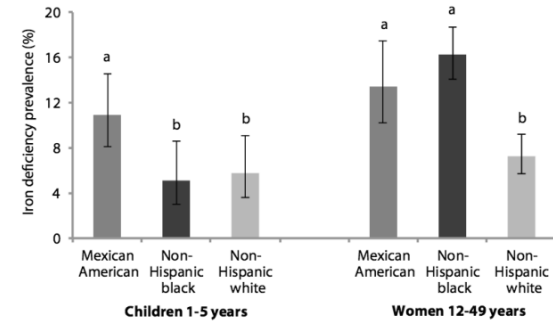


Figure H.3.a. Age-adjusted prevalence estimates of low body iron stores (<0 mg/kg) in U.S. children and women by race/ethnicity, National Health and Nutrition Examination Survey, 2003-2006.

Error bars represent 95% of confidence intervals. Bars are not sharing a common letter differ within children and women ($p < 0.05$). Age adjustment was done using direct standardization.

Viviana Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Recommended dietary allowances for iron for infants, children, and adult women

Age	Infants and children	Women	Pregnant	Breastfeeding
7 to 12 months	11 mg	n/a	n/a	n/a
1 to 3 years	7 mg	n/a	n/a	n/a
4 to 8 years	10 mg	n/a	n/a	n/a
9 to 13 years	8 mg	n/a	n/a	n/a
14 to 18 years	n/a	15 mg	27 mg	10mg
19 to 50 years	n/a	18 mg	27 mg	9 mg
51+ years	n/a	8 mg	n/a	n/a

Viviana Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

To Get 18mg of Iron in Food

- 4 cups of raisins
- 3-5 cups instant oatmeal
- 3 cups Special K cereal**
- 3 cups cooked lentils
- 2.2 cups canned white beans
- 10 ounce beef liver
- 45 ounce chicken breasts
- 15 cups broccoli OR
- 3 cups cooked spinach



Non heme iron absorption is 2- to 3-fold higher with co-ingestion of 25 to 75 mg of vitamin C

Viviana Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

Find Studies • About Studies • Submit Studies • Resources • About Site

Home • Search Results • Study Record Detail

Trial record 1 of 1 for: **BLOOD BUILDER**

Previous Study | Return to List | Next Study

Low-dose Iron Supplementation and Markers of Iron Status Among Non-anemic, Iron-deficient Women

This study is ongoing, but not recruiting participants.

Sponsor:
University of Maryland

Information provided by (Responsible Party):
Chris D'Adamo, University of Maryland

ClinicalTrials.gov Identifier:
NCT02683369

First posted: February 9, 2016
Last updated: March 26, 2017
Last verified: March 2017
History of Changes

Full Text View | Tabular View | No Study Results Posted | Disclaimer | How to Read a Study Record

Purpose

Healthy premenopausal women that are iron-deficient without anemia will receive a low-dose iron dietary supplement. The investigators seek to determine if the low-dose iron dietary supplement will restore iron levels to normal range with fewer side effects than typically experienced at higher doses of iron supplementation.

Condition	Intervention	Phase
Non-anemic Iron Deficiency	Dietary Supplement: Blood Builder/Iron Response®	Phase 2 Phase 3

Study Type: Interventional
Study Design: Interventional Model: Single Group Assignment
Masking: None (Open Label)
Primary Purpose: Treatment

Victoria Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Note: Hemochromatosis

- The gene for familial hemochromatosis (*HFE* gene) affects 8% of the US white population.
- Excess body iron is postulated to be important in the etiology of CAD, strokes, certain cancers, and neurodegenerative disorders because iron is important in free radical formation.
- Iron absorption is highly regulated to prevent excess, no physiologic pathway for ridding the body of iron exists.
- People NOT at risk of iron deficiency (teenage boys, adult men, women with infrequent menstrual cycles, and postmenopausal women) should NOT take multivitamins that contain iron or iron supplements unless instructed to do so by their health care provider.

Victoria Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Vitamin C: A Historical View

- The scourge of long voyage sailors, as many as 2/3rds of the crew would die of scurvy.
- Jacques Cartier 1535-6 in what is now Quebec city – cedar needles treated scurvy of men.
- James Lind, Scottish naval surgeon in 1747 found citrus fruit could treat and prevent scurvy
- Early 20th century many bottle fed babies died of scurvy. Pasteurized cow's milk destroys vitamin C.
- In the United States: 16 million Americans have very low serum vitamin C, many more have marginal status

Victoria Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

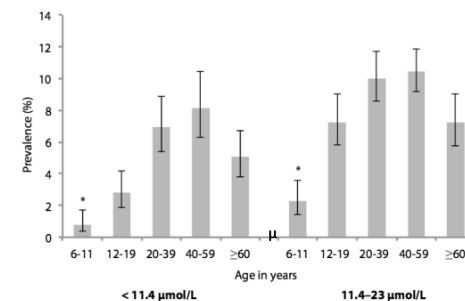


Figure H.1.f. Prevalence estimates of vitamin C deficiency (serum concentrations less than 11.4 µmol/L) and low vitamin C concentrations (11.4-23 µmol/L) in the U.S. population aged 6 years and older by age group, National Health & Nutrition Examination Survey, 2003-2006.

Error bars represent 95% of confidence intervals. *Prevalence in children is significantly lower than prevalence in persons 20 years and older ($p < 0.05$).

Victoria Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Food Source	Milligrams Vitamin C	Percent DV
Red pepper, sweet ½ cup	95	158%
Orange juice, ½ cup	93	155%
Orange, 1 medium	70	117%
Kiwifruit, 1 medium	64	107%
Broccoli, cooked, ½ cup	51	85%
Strawberries, fresh ½ cup	49	82%
Broccoli, raw ½ cup	39	65%
Cantaloupe, ½ cup	29	48%
Potato, baked 1 medium	17	28%
Tomato, raw 1 medium	17	28%
Spinach, cooked ½ cup	9	15%

DV = 60 mg

Vicenna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Vitamin C

- Potent **antioxidant**, activates folate, needed to convert tryptophan to serotonin, cofactor in synthesis of carnitine, thyroxine, norepinephrine, dopamine and immune cells
- Vitamin C levels **decline rapidly** during periods of emotional and physical strain, and illness.
- “Given the consistent effect of vitamin C on the duration and severity of colds in the regular supplementation studies, and the low cost and safety, it may be worthwhile for common cold patients to test on an individual basis whether therapeutic vitamin C is beneficial for them.”



Hemila H, et al. *Cochrane Database Syst Rev* 2013; Jan 31:1:CD 000980

Vicenna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Vitamin C Deficiency



- **Malaise and lethargy** early symptoms.
- Then **shortness of breath** and **muscle/bone pain**.
- **Skin changes, easy bruising, gum disease, loose teeth, slow healing wounds, dry mouth, dry eyes. emotionally labile.**
- **Weakened capillaries.** Hemorrhage is hallmark of scurvy and hair follicles are common site of cutaneous bleeding.
- **Inflammation of interdental and marginal gingiva followed by bleeding, ulceration, and bad breath.**
- **Swelling of periodontal membranes occur, followed by loss of bone and loosening of the teeth.**

Vicenna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Sperm

- Seminal fluid rich in vitamin C, acts as a potent antioxidant and helps to maintain the quality and function of sperm.
- **Fertile men have significantly higher seminal vitamin C levels compared to infertile men.**
- May improve sperm concentration and mobility.



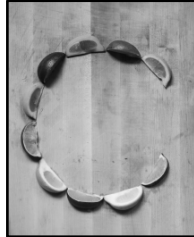
Rafiee B, et al. *Urol J* 2016; 13(2):2635-9.

Vicenna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Supplement Form

- Numerous forms of supplements available: calcium and mineral ascorbates, Ester-C, ascorbic acid and natural acerola/rose hips.
- Studies **have not found significant** differences between the different forms.
- **Oral dosing under tight control.**
- 200-300 mg in more frequent dosing is superior to larger single doses.



Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Upper Limits and Interactions

- Water soluble, **rapidly lost** if not continually replaced
- **Upper limit set at 2000 mg** because large doses cause loose stools and **mild gastrointestinal distress**. **Buffered forms** don't cause the gastrointestinal upset associated with just ascorbic acid.
- Those taking **anticoagulants** should **limit their vitamin C intake to 1 gram/day** and have their prothrombin time monitored.
- High doses can interfere with **interpretation of certain laboratory tests** (e.g., urine tests, guaiac test for occult blood, serum bilirubin, serum creatinine).

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Which of the following nutrients would be most beneficial for someone who has idiopathic taste disorders?

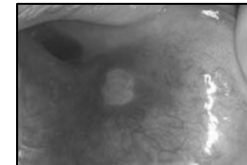
- Magnesium
- Vitamin C
- Zinc
- Biotin

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Zinc and Oral Health

- A review of clinical trials found “**moderate quality evidence** that **zinc supplements improve overall taste improvement in patients with zinc deficiency/idiopathic taste disorders.**”
- Zinc deficiency detected in 28% of recurrent aphthous stomatitis patients compared to controls.



Nagraj SK, et al. *Cochrane Database Syst Rev* 2014; 2014 Nov 26;11:CD010470.

Ozler GS. *J Laryngol Otol* 2014; 128(6):531-3

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Zinc and the Senses

- Zinc is necessary for **sense of smell**, which accounts for about 80% of your sense of taste!
- Also important for oral health; one sign of **zinc deficiency** is **red, swollen, and tender gums** that may bleed after brushing.
- Zinc helps protect cells that line the mouth in those undergoing chemotherapy or radiation.



Vicanna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Zinc and Taste

- Study found half of women undergoing chemotherapy for gynecological cancer experienced altered taste.
 - **Serum zinc consistently below lower limit of normal.**
- RDBPCT of adult patients with head and neck cancers received zinc sulfate (50 mg, three times a day) or placebo at start of radiation through one month post. **Zinc prevented radiation induced taste alterations.**

Nishijima S, et al. *Gynecol Oncol* 2013; 131(3):674-8.

Najafizade N, et al. *J Res Med Sci* 2013; 18(2):123-6

Vicanna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Zinc: Odds and Ends



- Men have higher daily requirement for production of **testosterone**, an important nutrient for male sexual maturation and reproduction.
- Zinc concentrations **very high in the prostate gland, testes, and in sperm**. Deficiency of this important trace mineral might contribute to lower testosterone and infertility in men.
- **Vegetarians** need 50% more zinc due to lower absorption of zinc from plant foods. DV= 15 mg
- **ACE inhibitors and thiazides deplete zinc**
- Take **2 hours apart from medication**, especially quinolones and tetracycline antibiotics.
- **Do not take > 40 mg/d** for more than a couple of months without supplementing copper. Daily value is 15 mg per day.

Vicanna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Table 2. Some Food Sources of Zinc

Food	Serving	Zinc (mg)
Oysters	6 medium (cooked)	27-50
Beef	3 ounces* (cooked)	3.7-5.8
Crab, Dungeness	3 ounces (cooked)	4.7
Pork	3 ounces (cooked)	1.9-3.5
Turkey (dark meat)	3 ounces (cooked)	3.0
Beans, baked	½ cup	0.9-2.9
Chicken (dark meat)	3 ounces (cooked)	1.6-2.7
Yogurt, fruit, nonfat	1 cup (8 fl. oz.)	1.8
Cashews	1 ounce	1.6
Chickpeas (garbanzo beans)	½ cup	0.5-1.3
Milk	1 cup (8 fl. oz.)	1.0
Almonds	1 ounce	0.9
Peanuts	1 ounce	0.9
Cheese, cheddar	1 ounce	0.9

*A three-ounce serving of meat is about the size of a deck of cards.

Vicanna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Calcium

- Calcium is a soft, grey metal, found in the bones and teeth of humans and animals in the form of calcium salts.
- Found in seashells and limestone—the word “calcium” is from Latin root for “lime.”
- Most abundant mineral in our body with roughly 99 percent of it stored in our bones, the rest is used to maintain healthy BP, nerve function and muscle contraction.



Vicenna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Calcium in Pregnancy



- Cochrane review found calcium supplementation roughly halves risk of pre-eclampsia; reduces risk of preterm birth and gestational HTN by roughly 35% compared to placebo.
- 1.0 – 1.5 grams/d calcium supplementation for those with low intake.

Hofmeyr GJ, et al. *Cochrane Database Syst Rev*. 2010 Aug 4;(8):CD001059.

Hofmeyr GJ, et al. *BJOG*. 2014 Mar 13. doi: 10.1111/1471-0528.

Whelan AM, et al. *Can J Clin Pharmacol* 2009; 16(3):e407-29.

Vicenna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

For every 2000 mg of sodium intake, it takes this much daily calcium, on average, to maintain calcium balance.

- A. 200 mg
- B. 500 mg
- C. 1000 m
- D. 1500 mg

Vicenna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Contributors to Lower Calcium

- One of the **first signs of calcium** deficiency is **muscle cramping**. Muscle aches of thighs and arms, with minimal exertion, could indicate a deficiency of calcium, vitamin D, and/or magnesium.
- Long term deficiency leads to **poor bone development/loss of bone mineral density, numbness and tingling in the fingers, convulsions, lethargy, poor appetite, and abnormal heart rhythms**.
 - Sodium: high sodium intake increases urinary calcium excretion. **1,000 mg/d of calcium per 2,000 mg/d sodium to maintain balance.**
 - **High protein intake** increases calcium excretion BUT it also increases absorption, overall, a **neutral** effect.
 - **Caffeine very modestly increases urinary excretion** (1 cup brewed coffee ~3 mg loss)
 - Alcohol can reduce calcium absorption and also reduce hepatic activation of vitamin D, by how much is unknown.

Vicenna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Calcium Calculator: A Quick Estimate

Food	# Servings/Day	Estimated Calcium per serving, in mg	Calcium in mg
Milk (8 ounces)		X 300	=
Yogurt (6 ounces)		X 300	=
Hard Cheese (1 ounce)		X 200	=
Soy milk, fortified (8 ounce)		X 300	=
Orange juice, fortified (8 ounce)		X 300	=
Tofu, firm calcium set (4 ounces)		X 300	=
All foods not included above		X 250	=
		Total Calcium	=
AI for your gender and age group		Subtract your total calcium from AI	= Supplement this amount

Vicanna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Calcium Requirements



- The RDA is 1,000 mg/day for children ages 4 to 8 years and 1,300 mg/day for boys and girls ages 9 to 13 years.
- Calcium intake recommendations are higher in children ages 9 to 13 to account for increased needs during puberty.
- Adults RDA is 1000 mg per day 1200 mg for women over 50 and 1200 mg for men over 70 years.

The National Academies Press, 2011:345-402.

Vicanna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Calcium supplement	Strength of each tablet (in milligrams)	Amount of elemental calcium per tablet (in milligrams)	Number of tablets to provide 1000 milligrams of calcium
Calcium carbonate	625	250	4
	650	260	4
	750	300	4
	835	334	3
	1250	500	2
	1500	600	2
Calcium citrate	950	200	5
Calcium gluconate	500	45	22
	650	58	17
	1000	90	11
Calcium lactate	325	42	24
	650	84	12
Calcium phosphate, dibasic	500	115	9
Calcium phosphate, tribasic	800	304	4

Vicanna

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Calcium and Vitamin D: Fracture

- Meta-analysis by National Osteoporosis Foundation: eight studies (n= 30,970 participants) found that **all studies showed calcium plus vitamin D supplementation produced a statistically significant 15 % reduced risk of total fractures and 30% reduced risk of hip fractures.**
- Dose of calcium ~1000 mg/d and vitamin D3 800 IU per day used in majority of studies.



Weaver CM, et al (2016). Calcium plus vitamin D supplementation and risk of fractures: an updated meta-analysis from the National Osteoporosis Foundation. *Osteoporosis Int*, 27: 367-376

Vicanna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Drug Induced Osteoporosis

- These drugs include:
 - Glucocorticoids (steroids) – 1:5 cases of osteoporosis
 - Aromatase inhibitors (breast cancer)
 - Anti-androgen therapy (prostate cancer)
 - Proton pump inhibitors (heartburn) – principally in those taking > 1 year (OR 4.55 for fracture if taking 7 or more years: should take calcium/vitamin D)
 - Antiretroviral drugs (HIV, hepatitis)
 - SSRIs (antidepressants) and antipsychotics
 - Antiepileptic (epilepsy, migraines, chronic pain, neuropathy)
 - Loop diuretics (e.g. lasix)
 - Heparin and oral anticoagulants



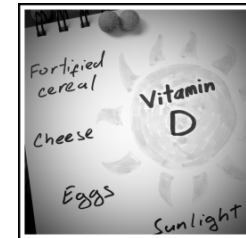
Mazzionti G, et al. *Am J Med* 2010; 123:877-84

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Vitamin D

- Vitamin D interacts with more than 1000 genes
- Vitrally important for calcium regulation (bones, heart, etc.)
- Higher blood levels improve breast cancer survival and reduce risk of colorectal cancer.
- Low vitamin D in adults causes muscle weakness and lower back and hip pain.
- Children with insufficient vitamin D at risk of developing hypomineralized dental enamel, increasing susceptibility to caries
- Obesity increases the risk of deficiency..



Kim Y, et al. *Br J Cancer* 2014; 110(11):2772-84.
Ma Y, et al. *J Clin Oncol* 2011; 29(28):3775-82

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

- Vitamin D deficiency is common worldwide but often more severe in elders due to environmental and biological factors.
- Impaired mobility often limits time spent outdoors and decreased synthesis of vitamin D in skin makes it difficult to maintain adequate levels even with sun exposure.
- As aging advances, intestinal resistance to 1,25(OH)2D impairs the uptake of calcium and a decline in renal function reduces activation of vitamin D.

Vitamin D



Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Fragility Fractures

- Fragility fractures are associated with decreased quality of life, increased disability, more frequent hospital admission and an increased risk of mortality.
- While a multimodal approach is important for fall protection, vitamin D supplementation alone, or in combination with calcium, has been shown to significantly reduce the risk of falling in elders.

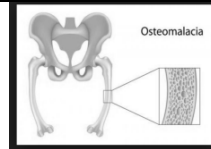


WHO. Nutrition for Older Persons.
<http://www.who.int/nutrition/topics/ageing/en/index.html> Accessed January 3, 2018

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Osteomalacia



- In adults, vitamin D deficiency can cause osteomalacia (lower bone mineralization), which can lead to musculoskeletal pain, usually in the pelvis, shoulders or proximal muscles.
- Pain increased by mild pressure on the sternum or anterior tibial bone are typical or suspected symptoms.
- Vitamin D has been shown to positively affect muscle strength, muscle size and neuromuscular performance.

Wintermeyer E, et al. Crucial Role of Vitamin D in the Musculoskeletal System. *Nutrients* 2016; Jun 1;8(6): pii: E319.

Victoria Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Vitamin D and Respiratory Infection



Martineau AR, et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. *BMJ* 2017; 356: e6583.

- Acute respiratory infection kills ~2.65 million people/year.
- 25 eligible randomized controlled trials (n=10,933, aged 0-95 years).
- Vitamin D supplementation reduced risk of acute respiratory infection among all participants (NNT=33) and those who were vitamin D deficient experienced the most benefit (NNT=4), as did those who were receiving daily or weekly vitamin D and *not* receiving vitamin D boluses (NNT=20).

Victoria Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Endocrine Society Guidelines

- Serum 25(OH)D level is used to determine vitamin D status
 - **Sufficiency** is 30 ng/mL (75 nmol/L) and above
 - **Insufficiency** defined as 21-29 ng/mL
 - **Deficiency** defined as <20 ng/mL
- **66.8 million Americans** 1 year and older had levels between **12-20 ng/ml**
- **23 million Americans** 1 year and older had levels **less than 12 ng/ml**
 - Most at risk were women and non-Hispanic blacks.

CDC 2nd National Report on Biochemical Indicators of Diet and Nutrition in the U.S. Population
Holick MF, et al. *J Clin Endocrinol Metab* 2011; 96(7):1911-30

Copyright Medicine Lodge Ranch, LLC. All rights reserved.

Victoria Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Endocrine Society Guidelines

“For clinical care, it appears that all current (testing) methodologies are adequate if one targets a 25(OH)D value higher than current cut points; *for example, a value of 40 ng/ml (100 nmol/L) is without toxicity and virtually ensures that the individuals ‘true’ value is greater than 30 ng/ml (75nmol/L).*”

Holick MF, et al. *J Clin Endocrinol Metab* 2011; 96(7):1911-30

Victoria Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Endocrine Society Guidelines for Treating Deficiency

All adults who are vitamin D deficient should be treated with **50,000 IU of vitamin D2/D3 once per week for 8 weeks** or 6000 IU of vitamin D2/D3 daily to achieve a blood level of 25(OH)D **above 30 ng/ml, followed by maintenance therapy of 1500–2000 IU/d.**



Holick MF, et al. *J Clin Endocrinol Metab* 2011; 96(7):1911-30

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Vitamin D

To get 600 IU/d Vitamin D3:

- 3-4 ounces sockeye salmon, cooked
- 11.4 ounces water-packed tuna
- 26 oil-packed sardines
- 15 large eggs
- 6 cups fortified milk OR
- 30-45 ounces yogurt

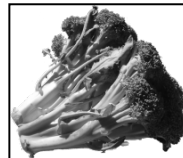
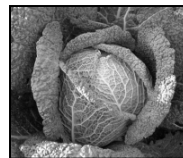


Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Vitamin K

- There are **two** main forms of vitamin K.
 - **Phylloquinone**, or vitamin **K1**, is synthesized by **plants** and makes up **90% of the vitamin K obtained in the diet**. Best sources are green leafy vegetables. Fat-soluble so should be eaten with some healthy fat.
 - **Menaquinone**, vitamin **K2**, is result of bacterial action in GI tract converting K1 to K2 or obtained directly from food sources such as meat, egg yolks, fermented dairy and soy (e.g., miso, natto).



Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Foods Highest in Vitamin K1

- Green leafy vegetables
 - Collards, kale, spinach, lettuce, mustard greens
- Cabbage type vegetables
 - Brussels sprouts, broccoli, green cabbage
- Avocado, kiwi, pickles
- Soybean, canola oils



Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Foods High in Vitamin K2

- Natto
- Hard cheese
- Soft cheese
- Egg yolk
- Butter (grass fed)
- Chicken liver
- Chicken breast
- Ground beef
- Fermented dairy/yogurt



Source: USDA

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

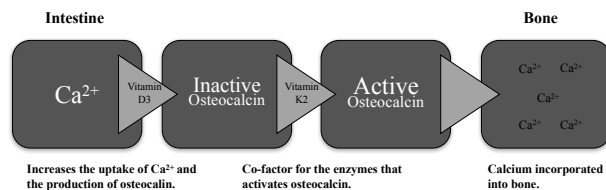
Vitamin K & Fracture

- 3 year trial of K2 (180 mcg/d) in postmenopausal women showed preservation of BMD in lumbar spine and slowed rate of bone loss in femoral neck.
- Meta-analysis of 19 RCTs (n=6759) “support the hypothesis that vitamin K2 plays role in the maintenance and improvement of vertebral BMD and the prevention of fractures in postmenopausal women with osteoporosis.”

Knapen MHJ, et al. *Osteoporosis Int.* 2013;24(9):2499-2507.

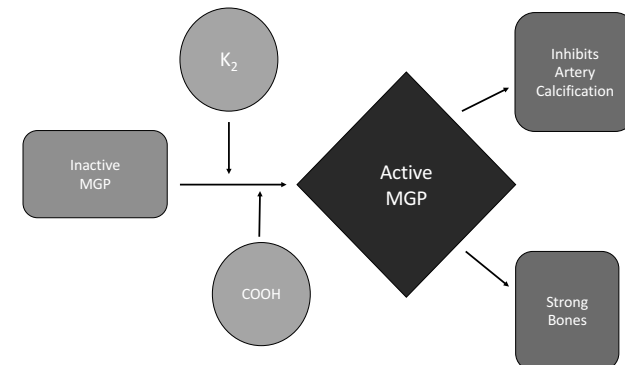
Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.



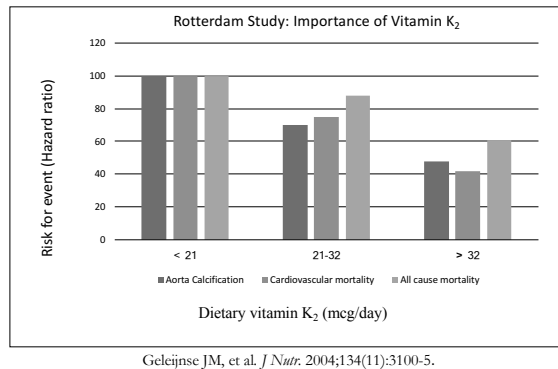
Vianna Low Dog, M.D.

Copyright © 2016 Integrative Medicine Concepts, LLC. All Rights Reserved.



Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.



Vicenna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

At Risk Populations

- Those who **don't regularly eat vegetables** and/or have **eliminated dairy and meat**.
- **Alcoholics**, anyone with a **digestive disorder** that impairs the **absorption of fats** (IBD, cystic fibrosis, etc.), those with **chronic liver disease** and possibly advanced kidney disease.
- In adults with **Crohn's disease**, 50-90% have vitamin K deficiency. In children, both Crohn's and ulcerative colitis lead to significant vitamin K deficiency.

Nowak JK, et al. *Sci Rep* 2014; 4: 4768

Vicenna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Vitamin K Deficiency

- **Bleeding** is the major symptom, especially in response to minor or trivial trauma.
- Any site can be involved, so manifestations can include mucosal and subcutaneous bleeding, such as **frequent nosebleeds, GI bleeding, heavy menstrual periods, hematuria, bleeding gums, and easy bruising**.
- **Long term**, vitamin K deficiency may cause **weak, brittle bones** and **increase calcifications** in blood vessels and soft tissues of the body.

Vicenna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Vitamin K Supplements

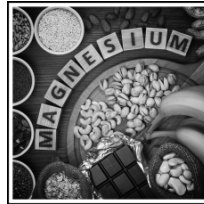
- Vitamin K **partners with vitamin D and calcium**, as well as **magnesium and zinc**.
- Supplements containing vitamin K1 and K2 may be optimal. Taking 100-300 mcg per day is usual.
- K2 has subtypes named **M (for menaquinone)**, **K (for vitamin K)**, followed by a number reflecting the number of prenyl units.
 - The two subtypes of most interest in human health are **MK-4 and MK-7**.

Vicenna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Magnesium

- **Low magnesium** intakes and serum levels associated with **type 2 diabetes, metabolic syndrome, inflammation, high blood pressure, atherosclerotic vascular disease, sudden cardiac death, osteoporosis, migraine headache, asthma, and colon cancer.**
- **50% of U.S. population** consumes less than the required amount of daily magnesium.
- Deficiency associated with negative effects on calcium and vitamin D homeostasis. **Magnesium required for the activation of vitamin D.**
- FDA requires warning that **proton pump inhibitors can cause dangerously low magnesium levels.**



Rosandff A, et al. *Nutr Rev* 2010;70(3):153-64

Copyright © Medicine Lodge Ranch, LLC
All rights reserved.

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC
All Rights Reserved

Magnesium: Diabetes and the Heart

- Higher magnesium intake associated with **lower risk of type 2 diabetes**, especially in the setting of poor carb-quality (high GL) diets.
- Meta-analysis found that circulating Mg levels are **inversely** associated with incidence of **coronary heart disease, hypertension, and type 2 diabetes.**
- Magnesium supplementation **300-400 mg per day** safe – caution in those with renal failure. At this time, **do not rely on topical application** of magnesium to raise mag levels.

Hruby A, et al. Magnesium Intake, Quality of Carbohydrates, and Risk of Type 2 Diabetes: Results From Three U.S. Cohorts. *Diabetes Care* 2017 Dec;40(12):1695-1702.

Wu J, et al. Circulating magnesium levels and incidence of coronary heart diseases, hypertension, and type 2 diabetes mellitus: a meta-analysis of prospective cohort studies. *Nutr J* 2017 Sep 19;16(1):60.

Grober U, et al. Myth or Reality-Transdermal Magnesium? *Nutrients* 2017 Jul 28;9(8).

Copyright © Medicine Lodge Ranch, LLC
All rights reserved.

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC
All Rights Reserved

Magnesium and Inflammation



- Low magnesium intake and low serum levels are associated with elevation in C-reactive protein. Individuals that are obese or have chronic diseases for which low-grade inflammation is a risk factor are commonly found to be magnesium-deficient.
- Correcting magnesium levels also shown to lower CRP.

Nielsen FH. *Curr Opin Clin Nutr Metab Care* 2014; 17(6):525-30.

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC
All Rights Reserved

FDA Safety Advisory

- FDA issued MedWatch warning and label change for PPIs due to low magnesium levels associated with long-term use.
- **“Those taking medications, generally more than one year, may end up with low magnesium, which can put them at risk for seizures, irregular heartbeats, and muscle spasms.”**
- Review of nine studies (n=115,455) found that the odds of *developing hypomagnesia increased by 75% if taking PPIs.*
- FDA advises magnesium levels be checked before and periodically during treatment.

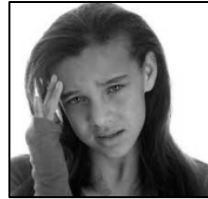
Park CH, et al. *PLoS One* 2014; Nov 13;9(11):e112558.

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC
All Rights Reserved

Magnesium for Migraines

- Studies show that migraineurs have **low brain Mg** during **migraine attacks** and may have **systemic Mg deficiency**.
- Mg reduces recurrent pediatric migraine and tension headaches.
- Canadian Headache Society **gave magnesium citrate a strong recommendation for prophylaxis of migraine**.
- Dose generally 300-600 mg/d. Diarrhea most common side effect (glycinate and citrate forms less GI complaints than oxide).



Sun-Edestein C, Mouskopoulos A. *Clin J Pain*. 2009 Jun;25(5):446-52.
 Pringsheim T, et al. *Can J Neurol Sci* 2012; 39(2Suppl):S1-S9
 Mouskopoulos A, et al. *J Neural Transm* 2012; 119(5):575-9.

Viviana Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Magnesium Deficiency

- People with magnesium deficiency may have **insulin resistance, menstrual cramps, leg cramps, migraines, fatigue, anxiety and mild elevations in blood pressure**.
- In **more severe cases** of deficiency, **seizures, tingling and numbness in the arms and legs, bizarre muscle movements (especially of the eyes and face), personality changes, and coronary spasms** can occur.
- Many medications can deplete magnesium (e.g., diuretics, PPIs, OCPs, gout medication, B2-agonists, steroids, etc.).

Viviana Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Thiamin and Diabetes

- **Altered glucose metabolism** associated with **lower thiamin** levels in diabetics, which in turn exacerbates hyperglycemia. Studies show that **diabetics often are thiamin deficient**.
- Simple sugars lack thiamin and metabolism of **high sugar foods** requires high amounts of thiamin and may accelerate its depletion.
- **Magnesium deficiency increases risk of thiamin deficiency** (need to make active form of thiamin (thiamin pyrophosphate))
- Studies suggest **thiamin supplementation may improve/slow/prevent microvascular complications of diabetes**.

Nix WA, et al. *Diabetes Res Clin Pract* 2015; 107(1):157-65.
 Alavi-Shahmiri F, et al. *Diabetes Metab Syndr* 2015; 9(4):213-7.
 Al Attas O, et al. *Clin Med Insights Endocrinol Diabetes* 2014; 7:1-6.

Viviana Low Dog, M.D.

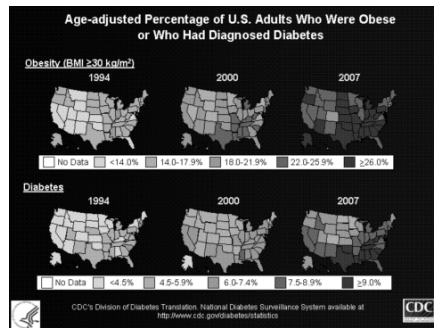
Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Deficiency

- **Reserves can be depleted within 2-3 weeks.**
- **Inadequate intake** (e.g., diet high in **polished rice, excessive sugars, inadequate intake of whole grains**)
- **Increased requirement** (adolescence, pregnancy, breastfeeding, athletes, diabetes, obesity, high carb diets, infection, hyperthyroidism, chemotherapy (5-FU), **low magnesium**)
- **Excessive loss** (diuretics, alcoholism, kidney dialysis, vomiting, **persistent diarrhea, diabetes**)
- **Consumption of anti-thiamin factors** (tea, coffee, betel nut, raw fish)
- **Intestinal malabsorption** (bypass, short gut syndrome, Crohn's disease, proton pump inhibitors)

Viviana Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.



Viviana Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Thiamin: Marginal Deficiency

- Thiamin found in **pork, beef, whole grains, organ meats, eggs, fish, legumes, and nuts**. Not present in fats/oils, polished rice, or simple sugars; dairy products, fruits and vegetables are not good source
- Studies suggest a myriad of vague signs and symptoms, including **mental fatigue and emotional lability, generalized weakness, myalgias, back pain, abdominal discomfort, poor memory, precordial pain, and a decreased ability to perform physical activity or work** can occur with marginal thiamin levels.
- **Virtually NO** clinician checks thiamin levels, though deficiency is well-documented in those who are obese and in diabetes.

Kerns JC, et al. *Adv Nutr* 2015; 6(2): 147-153

Viviana Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Partner Nutrients

- **Thiamin(e) is dependent upon magnesium**. Many people with diabetes and/or heart disease are **deficient in both**. These can also both be low in alcoholics – low magnesium may play a role in the hallucinations during alcohol withdrawal
- **B6, zinc, niacin and magnesium work together to convert the omega 3 ALA to DHA**.
- Works together with **calcium, zinc and vitamins D and K** for bone health.
- **If high risk deficiency: 10-100 mg per day**. No upper limit set by Food & Nutrition Board.

Viviana Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Iodine in Pregnancy

- Many reproductive aged women in US have marginal iodine status; **salt in processed foods is not iodized**.
- Deficiency associated with **pregnancy loss and prematurity, and neurocognitive defects in the baby**.
- Iodine deficiency now accepted as the most common cause of **preventable brain damage** in the world.
- Mild to moderate iodine deficiency associated with higher incidence of **ADHD and lower IQ** in the baby.
- American Thyroid Association recommends pregnant/lactating women supplement: **150 mcg/d potassium iodide**.



Council on Environmental Health, et al. *Pediatrics* 2014; 133(6):1163-6.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

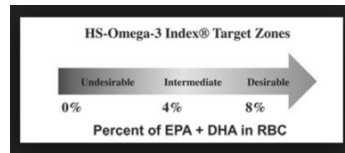
Viviana Low Dog, M.D.



Copyright © Integrative Medicine Concepts, LLC
All Rights Reserved

Copyright © Integrative Medicine Concept, LLC.
All Rights Reserved.

No Fish Story



- Omega-3 Index test is now the **gold standard for omega-3 biostatus** testing. It is used as a compliance marker for randomized controlled trials with fish oil supplements, and in epidemiological research.
- In 2008 Dr. Bernadine Healy, cardiologist and past President of the AHA and first woman Director of the NIH said, **“Before long, your personal Omega-3 Index just could be the new cholesterol—the number you want to brag about.”**
- Can order your own at requestatest.com

Copyright © Medicine Lodge Ranch, LLC
All rights reserved.

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC
All Rights Reserved.

Canadians and Omega 3: Not So Good

- The Omega-3 Index indicates the percentage of EPA+DHA in red blood cell fatty acids.
- Canadian government found that the mean Omega-3 Index level of Canadians aged 20-79 was 4.5%.
 - Levels higher for women, older adults, Asians and other non-white Canadians, omega-3 supplement users, and fish consumers; levels lower for smokers and people who were obese.
- **Fewer than 3% of adults had levels associated with low CHD risk; 43% had levels associated with high risk.**

Langlois K, et al. *Health Rep* 2015; Nov 18;26(11):3-11

Copyright © Medicine Lodge Ranch, LLC
All rights reserved.

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC
All Rights Reserved.

Omega 3 Fatty Acids – Healthy Muscles

- Chronic low-grade inflammation also contributes to the loss of muscle mass, strength and functionality, referred to as sarcopenia, as it affects both muscle protein breakdown and synthesis through several signaling pathways.
- Omega-3 fatty acids **stimulate muscle protein synthesis in older adults and may be useful for the prevention and treatment of sarcopenia.**



Dalle S, et al. *Front Physiol* 2017; Dec 12;8:1045
Ticinesi A, et al. *Nutrients* 2016; Mar 29;8(4):186

Copyright © Medicine Lodge Ranch, LLC
All rights reserved.

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC
All Rights Reserved.

Omega 3 and Prostate Cancer?

- SELECT trial raised concerns about potential link between omega 3s and increased prostate cancer/aggressive cancer.
- European Food Safety (EFSA) concluded, “there is **no evidence** for a role of EPA and/or DHA intake **in the development of prostate cancer.**”
- Also, **“supplemental intake of EPA and DHA combined at doses up to 5 g/d does not give rise to safety concerns for adults.”**
- **The FDA set the safe upper limit to 3 grams per day.**

EFSA Journal 10(7): doi:10.2903/j.efsa.2012.2815

Copyright © Medicine Lodge Ranch, LLC
All rights reserved.

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC
All Rights Reserved.

Omega 3 and Asthma

- Reduced intake of omega-3 fatty acids may be a contributing factor to the increasing prevalence of wheezing disorders.
- Reviewers found that supplementation with omega-3 fatty acids in the third trimester of pregnancy **reduced the absolute risk of persistent wheeze or asthma and infections of the lower respiratory tract in offspring by approximately 33%.**



Biggaard H, et al. *N Engl J Med* 2016; Dec 29;375(26):2530-9

Victoria Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Choose Your Seafood Wisely



<https://www.seafoodwatch.org/seafood-recommendations/our-app>

Copyright Medicine Lodge Ranch, LLC. All rights reserved.

Victoria Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Different Types of Fish Oil

- Supplementation is an alternative to eating fish; however, not all supplements are equal.
- Randomized, crossover study of 35 healthy individuals compared four popular brands/types of omega 3 fatty acids:
 - Concentrated triglyceride (rTG)
 - Ethyl ester (EE)
 - Phospholipid krill oil (PL)
 - Triglyceride salmon oil (TG)

Laidlaw M, et al. *Lipids Health Dis* 2014; 13:99

Victoria Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

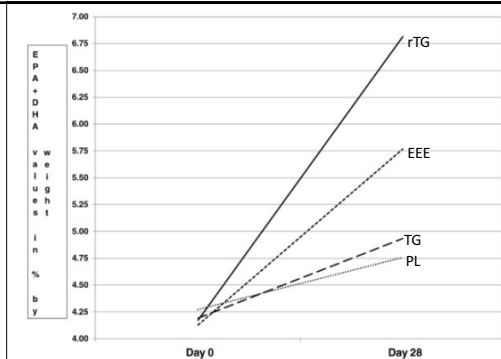
Dosing According to Manufacturer's Recommendations

TRT	Product	EPA & DHA per capsule*	Tested values	Label use: caps/day	Daily dosage of EPA + DHA
rTG	Nordic Naturals ProOmega®	325 mg EPA	329.6 mg EPA	2	EPA: 650 mg
	Triglyceride	225 mg DHA	226.0 mg DHA		DHA: 450 mg
EE	Minami MorEPA®	756 mg EPA	774.2 mg EPA	1	EPA: 756 mg
	Platinum Ethyl Ester	228 mg DHA	233.7 mg DHA		DHA: 228 mg
PL	Source Naturals ArcticPure®	75 mg EPA	78.0 mg EPA	2	EPA: 150 mg
	Krill Oil Phospholipid	45 mg DHA	46.7 mg DHA		DHA: 90 mg
TG	New Chapter				
	Wholemeg® Salmon	90 mg EPA	96.4 mg EPA	2	EPA: 180 mg
	Oil Triglyceride	110 mg DHA	109.5 mg DHA		DHA: 220 mg

Victoria Low Dog, M.D.

Copyright © 2016 Integrative Medicine Concepts, LLC. All Rights Reserved.

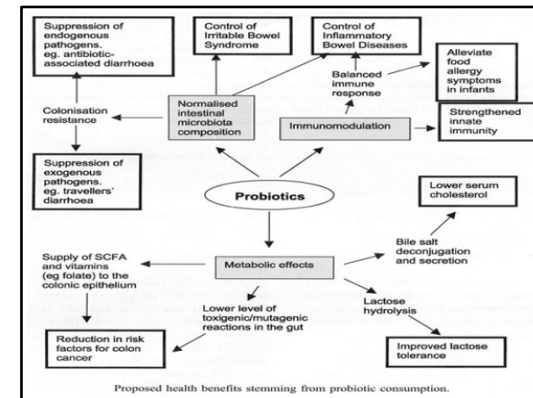
Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.



Mean levels of EPA + DHA for four supplement groups at Day 0 and Day 28.

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

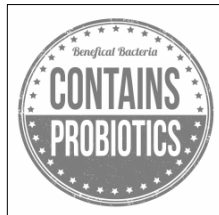


Proposed health benefits stemming from probiotic consumption.

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Probiotics and Prebiotics



Huo Q, Dong BR, Wu T. Probiotics for preventing acute upper respiratory tract infections. *Cochrane Database Syst Rev*. 2015 Feb 3;(2):CD006895.

- Probiotics **modulate innate and adaptive immunity in elderly and also reduce length of respiratory/flu infection in children and adults**
- Review of 12 studies with 3720 participants including children, adults, and older people not at high risk for URTI.
- Moderate-quality evidence shows number of **people who develop URTI is reduced when taking probiotics.**
- Moderate quality evidence probiotics **probably reduces duration of a URTI by approximately 2 days.**

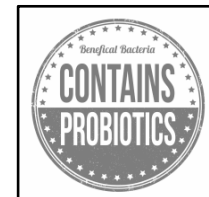
Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Probiotics and Oral Health

- A systematic review of probiotic strains for caries prevention showed promising results but only a few studies have demonstrated clear clinical outcomes.
- More than 14 strains have been researched.
- A continuous regular almost daily intake is probably required.



Cagetti MG, et al. *Nutrients* 2013; 5(7):2530-50

Vianna Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Evidence Based Products for Oral Health

INDICATION FOR ADULT HEALTH															
Brand Name	Probiotic Strain	Dosage Form	CFU/Dose	No of Doses/Day	ID	AAD	CDAD	TD	C	FAP	IBS	IBD-UC	IBD-P	HP	OH
Dentag™ Oral Health Probiotic Complex	<i>S. salivarius</i> BAA-1024 <i>L. plantarum</i> SO-5870 <i>L. reuteri</i> SD-5865 <i>L. acidophilus</i> SO-5212 <i>L. salivarius</i> SO-5209 <i>L. paracasei</i> SO-5273	Lozenge	1B/lozenge	2 lozenges											I 40-44
GumB PeriBalance®	<i>L. reuteri</i> ATCC 55730 100M <i>L. reuteri</i> ATCC PTA 5289 100M	Lozenge	200M/lozenge	2 lozenges											I 92,93
OralBiotics™ [BLIS K12]	<i>Streptococcus salivarius</i> K12	Lozenge	1B/lozenge	1-5 lozenges											I 50,51

® - Product requires refrigeration

usprobioticguide.com

Viviana Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Evidence Based Products for Oral Health

INDICATION FOR PEDIATRIC HEALTH															
Brand Name	Probiotic Strain	Dosage Form	CFU/Dose	No of Doses/Day	Regurg/Gi/Mot	Colic	ID	AAD	CDAD	IBD-UC	HP	C	FAP	IBS	OH
Dentag™ Oral and ENT Health Probiotic Complex	<i>S. salivarius</i> BAA-1024 <i>L. plantarum</i> SO-5870 <i>L. reuteri</i> SD-5865 <i>L. acidophilus</i> SO-5212 <i>L. salivarius</i> SO-5209 <i>L. paracasei</i> SO-5273	Lozenge	1B/lozenge	2 lozenges											I 40-44
OralBiotics™ [BLIS K12]	<i>Streptococcus salivarius</i> K12	Lozenge	1B/lozenge	1-5 lozenges											I 50,51

® - Product requires refrigeration

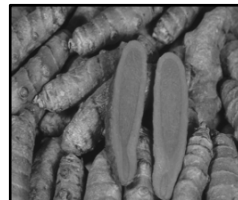
usprobioticguide.com

Viviana Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Turmeric Rhizome (*Curcuma longa* and others)

- Rhizomes provide bright yellow-orange culinary spice and dye.
- Yellow pigments = curcuminoids, one example is curcumin.
- Long history of medicinal use for respiratory, skin, digestive and inflammatory conditions in India.
- More than 65 clinical trials have shed light on its *potential* role in CVD, diabetes, cancer, fatty liver, arthritis, neuro/psych disorders.



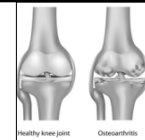
Kunnumakkara AB, et al. *Be J Pharmacol* 2016; Sep 17. doi: 10.1111/bjph.13621.

Prasad S, et al. *Biotechnol Adv* 2014; 32(6):1053-1064

Copyright © 2013 Integrative Medicine Concepts, LLC. All Rights Reserved.

Viviana Low Dog, M.D.

Turmeric: Osteoarthritis



- Research at the laboratory, translational and clinical levels supports use of curcumin for osteoarthritis.
- 4 week DB comparative study randomized 367 patients with knee OA to ibuprofen 1,200 mg/day or *C. domestica* extract (ethanolic) 1,500 mg/day (three divided doses).
- Curcumin as effective as ibuprofen for treatment of knee osteoarthritis based upon WOMAC scores.
- Abdominal discomfort significantly higher in ibuprofen group.

Peddada KV, et al. *Orthop Surg* 2015; 7(3):222-31

Kuptniratsaikul V, et al. *Clin Interv Aging* 2014; 9:451-8.

Viviana Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Turmeric for Depression?

- A mini meta-analysis of 6 studies found curcumin reduced depression symptoms, particularly in middle-aged patients when given at higher doses for longer periods of time.
- Authors concluded, “there is supporting evidence that curcumin administration reduces depressive symptoms in patients with major depression.”
- Is this an impact on microbiome? Is it due to systemic reduction in inflammation? *Intriguing.*



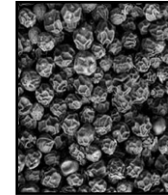
Al-Kawarni D, et al. *Phytother. Res* 2016; 30(2):175-83

Copyright © 2017 Integrative Medicine Concepts, LLC. All Rights Reserved.

Vicenna Low Dog, M.D.

Absorption and Safety Issues

- Low aqueous solubility of curcumin and its rapid metabolism and elimination from the body have constituted *major obstacles* to clinical use.
- Nanoencapsulation, curcumin complexed with phosphatidylcholine, and inclusion of the black pepper alkaloid, piperine, enhance tissue distribution and bioavailability.
- Note: Piperine causes inhibition of CYP3A4 and at doses of 20 mg can cause *clinically relevant drug interactions* especially for drugs with narrow therapeutic indices.
- Dose generally 1200-1800 mg per day of turmeric extract standardized to 95% curcumin, taken in divided doses.



Boddu SK, et al. *Drug Res* 2016; Oct 24

Gurley BJ, et al. *Planta Med* 2012; 78(13):1490-514

Copyright © 2017 Integrative Medicine Concepts, LLC. All Rights Reserved.

Vicenna Low Dog, M.D.

Read the Labels Carefully

Supplement Facts		
Serving Size: 1oz. Servings Per Container: 16		
	Amt. Per Serving	% Daily Value
Organic Turmeric Root Extract (Supercritical CO2 Extraction)	500mg *	
Organic Black Pepper Fruit Extract (Standardized to 95% Piperine)	10mg *	

Supplement Facts		
Serving Size: 1 Veggie Capsule Servings Per Container: 60		
Amount Per Serving	% Daily Value	
Turmeric (Curcuma Longa)(root)	600mg *	
Turmeric 95% Curcuminoids	50mg *	
* Daily Value not established		
Other Ingredients: Vegetable Cellulose (Veggie Cap).		

Copyright © 2017 Integrative Medicine Concepts, LLC. All Rights Reserved.

Vicenna Low Dog, M.D.

Vitamin and Mineral Deficiency: A Global Progress Report

“The control of vitamin and mineral deficiencies is one of the most extraordinary development-related scientific advances of recent years. Probably no other technology available today offers as large an opportunity to improve lives and accelerate development at such a low cost and in such a short time.”

The World Bank

www.unicef.org/media/files/vmd.pdf

Copyright © Integrative Medicine Concepts, LLC. All Rights Reserved.

Vicenna Low Dog, M.D.

Resources

- *Fortify Your Life*, Tieraona Low Dog, MD with National Geographic
- Dietary Supplement Label Database: dslid.nlm.nih.gov
- NIH National Center for Complementary and Integrative Health (NCCIH): nccih.nih.gov
- Office of Dietary Supplements: ods.od.nih.gov
- Linus Pauling Institute: lpi.oregonstate.edu
- Consumer Labs: www.ConsumerLabs.com
- Natural Medicines Comprehensive Database: NaturalDataBase.com

Tieraona Low Dog, M.D.

Copyright © Integrative Medicine Concepts, LLC.
All Rights Reserved.