## **Vitamin-Mineral Interactions**

By Deanna Minich, PhD

For many body processes to function optimally, you must have the right balance of essential nutrients. A deficiency in one might exacerbate a deficiency in another. Other nutrients are antagonists and may negatively impact the absorption of each other. The chart below indicates interactions among essential nutrients. Please note that this refers to high doses of nutrients; the moderate nutrient levels in multivitamins are not enough to trigger these interactions. For details on the interactions between these nutrients, read the full blog at DeannaMinich.com.

Nutrient	Synergistic Relationship	Varies Based on Nutrient Levels	Antagonistic Relationship
Vitamin A <sup>1-23</sup>	lodine, Iron, Zinc	Vitamin E	Vitamin K, Vitamin D
Vitamin B <sub>1</sub> 15, 24, 25 (Thiamin)	Magnesium		Vitamin B <sub>6</sub> ,
Vitamin B <sub>2</sub> 15 (Riboflavin)			Calcium
Vitamin B <sub>3</sub> <sup>26</sup> (Niacin)	Zinc		
Vitamin Bs <sup>15</sup> (Pantothenic acid)			Copper
Vitamin B <sub>6</sub> 15, 25, 27-36 (Pyridoxine)			Vitamin B <sub>1</sub> , Vitamin B <sub>9</sub> , Zinc
Vitamin B <sub>7</sub> 15, 25, 27-36 (Biotin)		Vitamin B₅	
Vitamin B <sub>9</sub> 15, 31, 39-43 (Folic acid)			Vitamin B <sub>6</sub> , Vitamin B <sub>12</sub> , Zinc
Vitamin B <sub>12</sub> 15, 39-41 (Cobalamin)			Vitamin B <sub>9</sub> , Vitamin C
Vitamin C 15,44-50	Vitamin E	Copper, Iron, Selenium	Vitamin B <sub>12</sub>
Vitamin D 1,51-60	Vitamin A, Vitamin K, Calcium, Magnesium, Selenium		Vitamin E,
Vitamin E 1-15, 44, 45, 61-65	Vitamin C, Selenium, Zinc	Vitamin A	Vitamin D, Vitamin K
Vitamin K <sup>1, 15, 51-55</sup>	Calcium	Vitamin D	Vitamin A, Vitamin E
Calcium 15, 55, 56, 65-83	Vitamin D, Potassium		Magnesium, Phosphorus, Sodium, Iron, Manganese, Zinc
Magnesium 57-60,74,84-86	Vitamin B <sub>1</sub> , Vitamin B <sub>6</sub> , Vitamin D, Potassium		Calcium, Phosphorus, Zinc
Phosphorus <sup>15, 77, 78, 86</sup>			Calcium, Magnesium
Potassium <sup>15, 69, 84, 87-94</sup>	Calcium, Manganese, Sodium		
Sodium <sup>69,79-81,87-94</sup>	Potassium		Calcium
Copper 15, 46, 50, 95-106		Vitamin C	Iron, Molybdenum, Selenium, Zinc
lodine <sup>15, 16, 110</sup>	Vitamin A, Selenium		
15, 18, 20, 47-49, 65, 70-73, 95, 111, 112	Vitamin A, Vitamin C		Vitamin E, Calcium, Copper, Manganese, Zinc
Manganese <sup>75,76,111,112</sup>			Calcium, Iron
Molybdenum <sup>94</sup>			Copper
Selenium 98, 110	Vitamin D, Vitamin E, Iodine	Vitamin C	Copper
Zinc <sup>15, 21-23, 26, 35, 36, 42, 43,</sup> 73, 82, 83, 85, 99-109	Vitamin A, Vitamin B₃		Calcium, Magnesium, Copper, Iron
Sulfur <sup>113</sup>	Molybdenum		

## References:

- Goncalves A et al. Fat-soluble vitamin intestinal absorption: absorption sites in the intestine and interactions for absorption. Food Chem. 2015;172:155-160.
- Egnell M et al. Antioxidant intake from diet and supplements and risk of digestive cancers in middle-aged adults: results from the prospective NutriNet-Santé cohort. Br. J Nutr. 2017;118(7):54-549.
- Dong Y, Liu Y, Shu Y et al. Link between risk of colorectal cancer and serum vitamin E levels: A meta-analysis of case-control studies. Medicine (Baltimore). 2017;96(27):e7470.
- Bakker MF et al. Plasma carotenoids, vitamin C, tocopherols, and retinol
  and the risk of breast cancer in the European Prospective Investigation
  into Cancer and Nutrition cohort. Am J Clin Nutr. 2016;103(2):454-464.
- Li L et al. Associations between micronutrient intakes and gut microbiota in a group of adults with cystic fibrosis. Clin Nutr. 2017;36(4):1097-1104.
- Godala MM et al. Lower plasma levels of antioxidant vitamins in patients with metabolic syndrome: a case control study. Adv Clin Exp Med. 2016;25(4):689-700.
- Doo M et al. The consumption of dietary antioxidant citamins modifies the risk of obesity among Korean men with short sleep duration. Nutrients. 2017;9(7):E780.
- Kim S et al. Total antioxidant capacity from dietary supplement decreases the likelihood of having metabolic syndrome in Korean adults. Nutrients. 2017;9(10):F1055.
- Elenius V et al. The relationship of serum vitamins A, D, E and LL-37 levels with allergic status, tonsillar virus detection and immune response. PLoS One. 2017;12(2):e0172350.
- Zhang X et al. Low serum levels of vitamins A, D, and E are associated with recurrent respiratory tract infections in children living in Northern China: a case control study. PLoS One. 2016;11(12):e0167689.
- Navarro P et al. Vegetable and fruit intakes are associated with hs-CRP levels in pre-pubertal girls. Nutrients. 2017;9(3):E224.
- Yang F et al. Dietary antioxidants and risk of Parkinson's disease in two population-based cohorts. Mov Disord. 2017;32(11):1631-1636.
- Raszewski G et al. Homocysteine, antioxidant vitamins and lipids as biomarkers of neurodegeneration in Alzheimer's disease versus non-Alzheimer's dementia. Ann Agric Environ Med. 2016;23(1):193-196.
- Curhan SG et al. Carotenoids, vitamin A, vitamin C, vitamin E, and folate and risk of self-reported hearing loss in women. Am J Clin Nutr. 2015;102(5):1167-1175.
- 15. Gaby AR. Nutritional medicine review. Glob Adv Health Med. 2013;2(1):80.
- Biebinger R et al. Effect of concurrent vitamin A and iodine deficiencies on the thyroid-pituitary axis in rats. Thyroid. 2006;16(10):961-965.
- Layrisse M et al. New property of vitamin A and beta-carotene on human iron absorption: effect on phytate and polyphenols as inhibitors of iron absorption. Arch Latinoam Nutr. 2000;50(3):243-248.
- García-Casal MN et al. Vitamin A and beta-carotene can improve nonheme iron absorption from rice, wheat and corn by humans. J Nutr. 1998:128(3):646-650.
- Kana-Sop MM et al. The influence of iron and zinc supplementation on the bioavailability of provitamin A carotenoids from papaya following consumption of a vitamin A-deficient diet. J Nutr Sci Vitaminol (Tokyo). 2015;61(3):205-214
- Al-Mekhlafi HM et al. Effects of vitamin A supplementation on iron status indices and iron deficiency anaemia: a randomized controlled trial. Nutrients. 2014;6(1):190–206.
- 21. Christian P, West KP Jr. Interactions between zinc and vitamin A: an update. *Am J Clin Nutr.* 1998;68(2 Suppl):4355-4415.
- Adriani M et al. The effect of adding zinc to vitamin A on IGF-1, bone age and linear growth in stunted children. J Trace Elem Med Biol. 2014;28(4):431-435.
- 23. Grahn BH et al. Zinc and the eye. J Am Coll Nutr. 2001;20(2).
- Itokawa Y et al. Changes in tissue magnesium, calcium and phosphorus levels in magnesium-deficient rats in relation to thiamin excess or deficiency. J Nutr. 1973;103(3):438-443.
- Lewin LM et al. The biosynthesis of thiamine. IV. Inhibition by vitamin B<sub>6</sub> compounds. Arch Biochem Biophys. 1963;101:197-203.
- Tupe RS et al. Dietary nicotinic acid supplementation improves hepatic zinc uptake and offers hepatoprotection against oxidative damage. Br J Nutr. 2011;105(12):1741-1749.
- Abraham GE et al. Effect of vitamin B-6 on plasma and red blood cell magnesium levels in premenopausal women. *Ann Clin Lab Sci.* 1981;11(4):333-336.
- Planells E et al. Effect of magnesium deficiency on vitamin B2 and B6 status in the rat. J Am Coll Nutr. 1997;16(4):352-356.
- Fathizadeh N et al. Evaluating the effect of magnesium and magnesium plus vitamin B6 supplement on the severity of premenstrual syndrome. Iran J Nurs Midwifery Res. 2010;15(Suppl 1):401-405.
- Martineau J et al. Vitamin B6, magnesium, and combined B6-Mg: therapeutic effects in childhood autism. Biol Psychiatry. 1985;20(5):467-478.
- Naurath HJ et al. Does a single vitamin B-supplementation induce functional vitamin B-deficiency? Clin Chem Lab Med. 2001;39(8):768-771.
- Lobo A et al. Reduction of homocysteine levels in coronary artery disease by low-dose folic acid combined with vitamins B6 and B12. Am J Cardiol. 1999;83(6):821-825.
- Undas A et al. Treatment of hyperhomocysteinemia with folic acid and vitamins B12 and B6 attenuates thrombin generation. *Thromb Res.* 1999;95(6):281-288.
- Kalani A et al. Nutri-epigenetics ameliorates blood-brain barrier damage and neurodegeneration in hyperhomocysteinemia: role of folic acid. J Mol Neurosci. 2014;52(2):202-215.
- Turnlund JR et al. A stable-isotope study of zinc, copper, and iron absorption and retention by young women fed vitamin B-6-deficient diets. Am J Clin Nutr. 1991;54(6):1059-1064.
- Prasad R et al. Effect of vitamin B6 and B1 deficiencies on the intestinal uptake of calcium, zinc and cadmium. Ann Nutr Metab. 1982;26(5):324-330.
- 37. Tripathy S et al. Interrelationship of micronutrients: antagonism and synergism. *Int. J Pure App Biosci.* 2017;5(6):208-214.
- Linus Pauling Institute. Biotin. https://lpi.oregonstate.edu/mic/vitamins/ biotin. Accessed September 6, 2018.

- 39. Hughes CF et al. Vitamin B12 and ageing: current issues and interaction with folate. *Ann Clin Biochem*. 2013;50(Pt 4):315-329.
- Shen L et al. Associations between homocysteine, folic acid, vitamin B12 and Alzheimer's disease: insights from meta-analyses. J Alzheimers Dis. 2015;46(3):777-790
- National Health Service. Vitamin B12 or folate deficiency anaemia. https:// www.nhs.uk/conditions/vitamin-b12-or-folate-deficiency-anaemia/. Accessed January 31, 2018.
- 42. Hansen M et al. Folic acid enrichment of bread does not appear to affect zinc absorption in young women. *Am J Clin Nutr.* 2001;74(1):125-129.
- Milne DB et al. Effect of oral folic acid supplements on zinc, copper, and iron absorption and excretion. Am J Clin Nutr. 1984;39(4):535-539.
- Chen LH. Interaction of vitamin E and ascorbic acid (review). In Vivo. 1989;3(3):199-209.
- Niki E, et al. Interaction among vitamin C, vitamin E, and beta-carotene Am J Clin Nutr. 1995:62(6 Suppl):13225-13265.
- Harris ED et al. A role for ascorbic acid in copper transport. Am J Clin Nutr 1991;54(6 Suppl):1193S-1197S.
- Lynch SR et al. Interaction of vitamin C and iron. Ann NY Acad Sci. 1980;355:32-44.
- Teucher B et al. Enhancers of iron absorption: ascorbic acid and other organic acids. Int J Vitam Nutr Res. 2004;74(6):403-419.
- Lane DJ et al. The active role of vitamin C in mammalian iron metabolism: much more than just enhanced iron absorption! Free Radic Biol Med. 2014;75:69-83.
- Van den Berg GJ et al. Influence of ascorbic acid supplementation on copper metabolism in rats. Br J Nutr. 1992;68(3):701-715.
- Healthline. Is Vitamin D Harmful Without Vitamin K? https://www.healthline.com/nutrition/vitamin-d-and-vitamin-k#section2. Accessed January 31, 2018.
- van Ballegooijen AJ et al. The synergistic interplay between vitamins D and K for bone and cardiovascular health: a narrative review. Int J Endocrinol. 2017;7454376.
- Karamali M et al. The effects of calcium, vitamins D and K co-supplementation on markers of insulin metabolism and lipid profiles in vitamin D-deficient women with polycystic ovary syndrome. Exp Clin Endocrinol Diabetes. 2017;125(5):316-321.
- van Ballegooijen AJ et al. Joint association of low vitamin D and vitamin K status with blood pressure and hypertension. *Hypertension*. 2017;69(6):1165-1172.
- Khazai N et al. Calcium and vitamin D: skeletal and extraskeletal health. Curr Rheumatol Rep. 2008;10(2):110-117.
- Thacher TD et al. Vitamin D treatment in calcium-deficiency rickets: a randomised controlled trial. Arch Dis Child. 2014;99(9):807-811.
- Al-Daghri NM et al. Vitamin D supplementation and serum levels of magnesium and selenium in type 2 diabetes mellitus patients: gender dimorphic changes. Int J Vitam Nutr Res. 2014;84(1-2):27-34.
- Farhanghi MA et al. Obesity induced magnesium deficiency can be treated by vitamin D supplementation. J Pak Med Assoc. 2009;59(4):258-261.
- Rosanoff A et al. Essential nutrient interactions: does low or suboptimal magnesium status interact with vitamin D and/or calcium status? Adv Nutr. 2016;7(1):25-43.
- Deng X et al. Magnesium, vitamin D status and mortality: results from US National Health and Nutrition Examination Survey (NHANES) 2001 to 2006 and NHANES III. BMC Med. 2013;11:187.
- 61. Hill KE et al. Combined selenium and vitamin E deficiency causes fatal myopathy in guinea pigs. *J Nutr.* 2001;131(6):1798-1802.
- Reagan-Shaw S et al. Combination of vitamin E and selenium causes an induction of apoptosis of human prostate cancer cells by enhancing Bax/ Bcl-2 ratio. Prostate. 2008;68(15):1624-1634.
- Bartfay WJ et al. The synergistic effects of vitamin E and selenium in iron-overloaded mouse hearts. Can J Cardiol. 1998;14(7):937-941.
- Zu K et al. Synergy between selenium and vitamin E in apoptosis induction is associated with activation of distinctive initiator caspases in human prostate cancer cells. Cancer Res. 2003;63(20):6988-6995.
- Omara FO et al. Vitamin E is protective against iron toxicity and iron-induced hepatic vitamin E depletion in mice. J Nutr. 1993;123(10):1649-1655
- Bolton-Smith C et al. Two-year randomized controlled trial of vitamin K1 (phylloquinone) and vitamin D3 plus calcium on the bone health of older women. J Bone Miner Res. 2007;22(4):509-519.
- Mayer O Jr et al. Synergistic effect of low K and D vitamin status on arterial stiffness in a general population. J Nutr Biochem. 2017;46:83-89.
- Asemi Z et al. The effects of vitamin D, K and calcium co-supplementation on carotid intima-media thickness and metabolic status in overweight type 2 diabetic patients with CHD. Br J Nutr. 2016;116(2):286-293.
- Turner KM et al. Sodium and potassium excretion are related to bone mineral density in women with coeliac disease. Clin Nutr. 2015;34(2):265-268.
- Bendich A. Calcium supplementation and iron status of females. Nutrition. 2001;17(1):46-51.
- Ríos-Castillo I et al. One-month of calcium supplementation does not affect iron bioavailability: a randomized controlled trial. Nutrition 2014;30(1):44-48.
- Walczyk T et al. Inhibition of iron absorption by calcium is modest in an iron-fortified, casein- and whey-based drink in Indian children and is easily compensated for by addition of ascorbic acid. J Nutr. 2014;144(11):1703-1709.
- Jayalakshmi S et al. Compromised zinc status of experimental rats as a consequence of prolonged iron & calcium supplementation. *Indian J Med Res*. 2016;143(2):238-244.
- de Swart PM et al. The interrelationship of calcium and magnesium absorption in idiopathic hypercalciuria and renal calcium stone disease J Urol. 1998;159(3):669-672.
- Davidsson L et al. The effect of individual dietary components on manganese absorption in humans. Am J Clin Nutr. 1991;54(6):1065-1070.
- Lutz TA et al. Effects of calcium and sugars on intestinal manganese absorption. Biol Trace Elem Res. 1993;39(2-3):221-227.
- Calvo MS et al. Is phosphorus intake that exceeds dietary requirements a risk factor in bone health? Ann NY Acad Sci. 2013;1301:29-35.

- Hall DD et al. Effects of dietary calcium, phosphorus, calcium: phosphorus ratio and vitamin K on performance, bone strength and blood clotting status of pigs. J Anim Sci. 1991,69(2):646-655.
- Nordin BE et al. The nature and significance of the relationship between urinary sodium and urinary calcium in women. J Nutr. 1993;123(9):1615-1622.
- Park SM et al. Effect of high dietary sodium on bone turnover markers and urinary calcium excretion in Korean postmenopausal women with low bone mass. Eur J Clin Nutr. 2015;69(3):361-266.
- Matkovic V et al. Urinary calcium, sodium, and bone mass of young females. Am J Clin Nutr. 1995;62(2):417-425.
- Suzuki T et al. Zinc deficiency increases serum concentrations of parathyroid hormone through a decrease in serum calcium and induces bone fragility in rats. J Nutr Sci Vitaminol. 2015;61:382-390.
- O'Dell BL et al. Impaired calcium entry into cells is associated with pathological signs of zinc deficiency. Adv Nutr. 2013;4(3):287-293.
- Adebamowo SN et al. Association between intakes of magnesium, potassium, and calcium and risk of stroke: 2 cohorts of US women and updated meta-analyses. Am J Clin Nutr. 2015;101(6):1269-277.
- Spencer H et al. Inhibitory effects of zinc on magnesium balance and magnesium absorption in man. J Am Coll Nutr. 1994;13(5):479-484.
- Brink EJ et al. Interaction of calcium and phosphate decreases ileal magnesium solubility and apparent magnesium absorption in rats. J Nutr. 1992;122(3):580-586.
- Perez V et al. Sodium-to-potassium ratio and blood pressure, hypertension, and related factors. Adv Nutr. 2014;5(6):712-741.
- Zhao X et al. Associations of urinary sodium and sodium to potassium ratio with hypertension prevalence and the risk of cardiovascular events in patients with prehypertension. *J Clin Hypertens* (Greenwich). 2017;19(12):1231–1239.
- Xu J et al. Associations of usual 24-hour sodium and potassium intakes with blood pressure and risk of hypertension among adults in China's Shandong and Jiangsu provinces. Kidney Blood Press Res. 2017;42(1):188-200.
- Chmielewski J et al. Dietary sodium, dietary potassium, and systolic blood pressure in US adolescents. J Clin Hypertens (Greenwich). 2017;19(9):904-909.
- Willey J et al. Dietary Sodium to Potassium Ratio and Risk of Stroke in a Multiethnic Urban Population: The Northern Manhattan Study. Stroke. 2017;48(11):2979-2983.
- Cao WT et al. The association between urinary sodium to potassium ratio and bone density in middle-aged Chinese adults. Osteoporos Int. 2017;28(3):1077-1086.
- Jain N et al. Association of urinary sodium-to-potassium ratio with obesity in a multiethnic cohort. Am J Clin Nutr. 2014;99(5):992-998.
- Williams RS et al. The role of dietary acid load and mild metabolic acidosis in insulin resistance in humans. *Biochimie*. 2016;124:171-177.
- 95. Arredondo M et al. Inhibition of iron and copper uptake by iron, copper and zinc. *Biol Res.* 2006;39(1):95-102.
- Flores CR et al. Trace elements status in diabetes mellitus type 2: possible role of the interaction between molybdenum and copper in the progress of typical complications. *Diabetes Res Clin Pract*. 2011;91(3):333-341.
- Yu S et al. The lowering effect of high copper intake on selenium retention in weanling rats depends on the selenium concentration of the diet. J Anim Physiol Anim Nutr (Berl). 2001;85(1-2):29-37.
- Ozturk P et al. Copper/zinc and copper/selenium ratios, and oxidative stress as biochemical markers in recurrent aphthous stomatitis. *J Trace Elem Med Biol.* 2013;27(4):312-316.
- National Institutes of Health. Zinc Fact Sheet. https://ods.od.nih.gov/ factsheets/Zinc-Health Professional. Accessed January 31, 2018.
- Linus Pauling Institute. Oregon State University. Micronutrient Information Center: Copper. http://pi.oregonstate.edu/mic/minerals/copper.
   Accessed January 31, 2018.
- Mezzetti A et al. Copper/zinc ratio and systemic oxidant load: effect of aging and aging-related degenerative diseases. Free Radic Biol Med. 1000/1616/2016
- Malavolta M et al. Plasma copper/zinc ratio: an inflammatory/nutritional biomarker as predictor of all-cause mortality in elderly population. Biogerontology. 2010;11(3):309-319.
- Jarosz M et al. Antioxidant and anti-inflammatory effects of zinc.
   Zinc-dependent NF-xB signaling. Inflammopharmacology. 2017;25(1):11-24.
- Luojus MK et al. Serum copper, zinc and high-sensitivity C-reactive protein in short and long sleep duration in ageing men. J Trace Elem Med Biol. 2015;32:177-182
- 105. Viktorinova A et al. Changed plasma levels of zinc and copper to zinc ratio and their possible associations with parent- and teacher-rated symptoms in children with attention-deficit hyperactivity disorder. Biol Trace Elem Res. 2016;169(1):1-7
- Alexanian I et al. Clinical and echocardiographic correlates of serum copper and zinc in acute and chronic heart failure. Clin Res Cardiol. 2014;103(11):938-949.
- 107. Younesi S et al. Dyshomeostasis of serum oxidant/antioxidant status and copper, zinc, and selenium levels in elderly physically disabled persons: an AHAP-based study. Biol Trace Elem Res. 2015;166(2):136-141.
- Lin CC et al. Trace elements, oxidative stress and glycemic control in young people with type 1 diabetes mellitus. J Trace Elem Med Biol. 2014;28(1):18-22.
- Li SO et al. Serum copper and zinc levels in individuals with autism spectrum disorders. Neuroreport. 2014;25(15):1216-1220.
- 110. Hotz CS et al. Dietary iodine and selenium interact to affect thyroid hormone metabolism of rats. *J Nutr.* 1997;127(6):1214-1218.
- Davis CD et al. Varying levels of manganese and iron affect absorption and gut endogenous losses of manganese by rats. J Nutr. 1992;122(6):1300-1308.
- Rossander-Hultén L et al. Competitive inhibition of iron absorption by manganese and zinc in humans. Am J Clin Nutr. 1991;54(1):152-156.
- Linus Pauling Institute. Molybdenum. https://lpi.oregonstate.edu/mic/ minerals/molybdenum. Accessed September 6, 2018.

