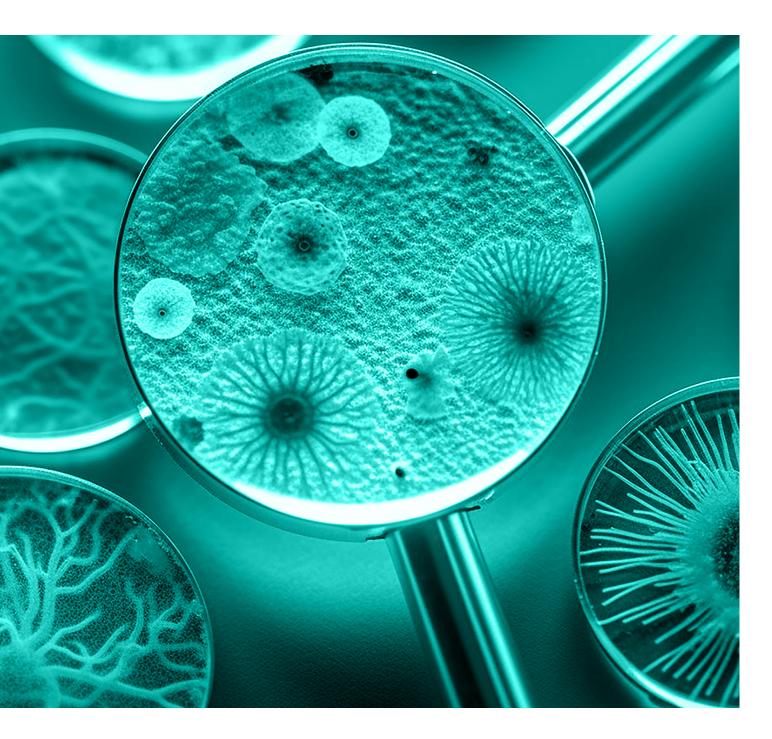


CANXIDA REBUILD

WHITE PAPER





The aim of this white paper is to provide an overview of Candida, its impact on nutrient absorption, and how using CanXida Rebuild (RBD) can treat resultant nutrient deficiency. The nutrients impacted by Candida overgrowth will be reviewed in addition to the role of multivitamin replenishment in recovery. Lastly, a breakdown of the vitamins and minerals contained in CanXida Rebuild RBD and their importance will be described, with a particular focus on their role in immune function.

INTRODUCTION

The gastrointestinal (GI) tract is the site of nutrient absorption from dietary intake. The ability of our body to absorb and use available nutrients depends on various factors such as diet¹, stomach acidity², medication³, and age⁴, among others. The diverse ecosystem of bacteria, fungi, and viruses that live in the GI tract, known collectively as the gut microbiome, also plays a central role in nutrient absorption⁵. The microbiome varies from person to person, which means that each individual has different nutrient absorption capabilities. As such, factors that impact microbiome diversity, like antibiotics and diet, also impact nutrient uptake.

Microbiome dysregulation, such as overgrowth of opportunistic fungal pathogens of the genus Candida, can impact nutrient availability. Indeed, many important nutrients are reduced in the bodies of patients with a Candida infection (candidiasis)⁶. Crucially, many of these nutrients are important for proper immune function. Thus, their depletion aids Candida pathogenicity. Replenishing levels of these nutrients is therefore key to recovering from Candida overgrowth.

NUTRIENTS IMPACTED BY CANDIDA OVERGROWTH

Many essential nutrients are depleted in patients with Candida overgrowth⁶. These nutrients play diverse roles in our bodies, including immune responses. These are described below.

MAGNESIUM

Magnesium is essential for many enzymatic reactions including most vitamin B6 reactions⁷ and is abundant in leafy green vegetables. Lack of magnesium, known as hypomagnesemia, causes neuromuscular dysfunction and increased risk of infection and cancer⁸. Within the immune system, magnesium contributes to the activation of T-cells, a diverse set of immune cells involved in the response to Candida. Individuals with GI disease are considered at risk for developing magnesium deficiencies due to impeded absorption⁹. Depletion of magnesium disrupts mineral homeostasis and is often accompanied by calcium and potassium deficiency⁷.

VITAMIN B6

Vitamin B6 comprises six molecules with similar functions and is abundant in many foods such as chickpeas, beef liver, and a variety of fish. Vitamin B6 is absorbed in the jejunum of the small intestine and is essential for around 150 biochemical reactions in the body. Deficiency of vitamin B6 is usually accompanied by deficiencies in other vitamins and causes neurocognitive and immune dysfunction, among other conditions¹⁰. It is essential for a functional immune system, and supplementation with vitamin B6 has been shown to improve T-cell differentiation, a necessary component of immune activity¹¹.

ZINC

Zinc is an essential mineral involved in many physiological functions and is abundant in red meat, oysters, and cereals (which are often fortified with zinc)¹⁰. The small intestine is the site of zinc absorption and deficiency accompanies many diseases. Many GI diseases reduce zinc absorption and zinc supplementation has been found to improve epithelial barrier function in the small intestine which means that the gut is less leaky and susceptible to infection¹². Zinc deficiency causes immune dysfunction, with studies documenting early deaths associated with infection in zinc-deficient populations¹³.

canxida

RIBOFLAVIN

Also known as vitamin B2, riboflavin is an essential cofactor for two coenzymes; flavin mononucleotide and flavin adenine dinucleotide. These coenzymes are essential for allowing cells to make energy and for antibody production via the metabolism of other B-group vitamins¹⁴. Commonly found in beef, yogurt, and fortified cereals, riboflavin is primarily absorbed in the small intestine, however, absorption can also occur at other GI locations¹⁵. Riboflavin deficiency is primarily caused by dietary insufficiency, though GI diseases are also implicated¹⁶.

IRON

An essential nutrient, primarily associated with its role in oxygen transport in hemoglobin, iron is also key for other cellular functions like DNA synthesis and cellular energy production. Iron is abundant in red meat and lentils and is primarily absorbed in the small intestine¹⁷. Its absorption can be inhibited by dietary factors and GI diseases, including many types of infection¹⁸. Iron deficiency causes anemia and affects immune function. It contributes to the function of a variety of immune cells including macrophages and neutrophils both of which work, in part, by eating microbial pathogens¹⁹.

FOLATE

Folate, also known as vitamin B9, is an essential nutrient involved in processes like DNA synthesis. Its name is derived from the Latin word for leaf, folium, and is found in leafy green vegetables like spinach¹⁰. Folate is particularly important in bodily processes requiring rapid cellular proliferation. Thus, folate deficiency is associated with birth defects²⁰. It is primarily absorbed in the small intestine²¹ where inflammatory diseases affect its absorption. Immune responses trigger rapid expansion of T-cell populations, and folate is believed to be important for this process²².

VITAMIN A

Vitamin A is an important set of nutrients found in a variety of foods and is important for many physiological functions including vision and immune responses¹⁰. Like other fat-soluble vitamins, it is absorbed in the upper GI tract. Vitamin A deficiency can cause, among other conditions, visual impairment, compromised immune responses, and susceptibility to epithelial infection caused by reduced mucus production²³. During immune responses, vitamin A plays a role in the proliferation and differentiation of T-cells and indirectly affects antibody production²⁴.

CALCIUM

Calcium is a nutrient involved in a plethora of structural and signaling functions and is abundant in dairy products and certain vegetables¹⁰. It is mostly absorbed in the small intestine where vitamin D plays a major role in its absorption²⁵. Calcium deficiency can lead to osteoporosis, rickets, and other bone diseases. In the immune system, calcium plays complex roles²⁶, including T-cell activation²⁷.

VITAMIN C

Vitamin C is an essential nutrient abundant in citrus fruits, but also in kale and green chili peppers²⁸. It is important for many biochemical processes and functions including tissue repair and immune responses. It is absorbed in the small intestine and vitamin C plasma levels are adversely affected by many diseases including GI infections²⁸. Specific roles within the immune system include triggering of neutrophil migration to the site of infection and neutrophil clearance by macrophages²⁹.

canxida

REPLENISHING WITH MULTIVITAMINS

THE ROLE OF VITAMINS AND MINERALS IN RECOVERY

Immune suppression is a risk factor for candidiasis³⁰. Since candidiasis is associated with the depletion of many essential nutrients, it is important to strengthen the immune system by supplementing with these missing vitamins and minerals during recovery. Prolonged nutrient depletion leaves the body susceptible to renewed infection.

The clearance of pathogenic microorganisms is only one part of an immune response. The expanded repertoire of T-cells and B-cells must be culled by specialized immune cells once the infection is cleared. Additionally, damages to tissue because of inflammation or direct attack by pathogens must be remedied through an immune system-mediated response called wound healing³¹. For specific examples consider zinc and vitamin C.

Zinc has been suggested to play a role in the repair of the epithelial layer in the context of colitis, though epithelial damage is also a feature of invasive candidiasis. Researchers found that a zinc-dependent protein known as Krüppel-like factor 5 was important for epithelial repair via increasing cellular proliferation and migration³².

Vitamin C has been shown to reduce wound healing time in patients, and as such, post-surgery patients are commonly treated with large doses of vitamin C³³. At the molecular level, vitamin C acts by preventing the auto-inactivation of enzymes that are required for collagen formation³⁴. There is also evidence to suggest that vitamin C promotes the stability of collagen mRNA thereby increasing its abundance³⁵. Collagen is a central component of many human tissues, it is therefore used as a primary building block during tissue repair.

HOW CANDIDA INFECTION REDUCES UPTAKE ABILITY

Candida sequesters several important nutrients from its local environment to allow itself to grow and survive or to defend itself from immune cells. In doing so, Candida renders these nutrients unavailable for use by the host.

Candida albicans (C. albicans), the most common pathogenic species of the Candida genus, is able to assimilate many sources of carbon, while other yeast species like Saccharomyces cerevisiae are only able to use glucose. Importantly, certain immune cells are also only capable of using glucose. This is important because C. albicans can indirectly trigger immune cell death by depleting the local environment of glucose, C. albicans can then switch to another source of carbon in an immune-depleted environment³⁶.

Another nutrient that Candida species deprive their host of is iron. Indeed, Candida has been shown to take part in a process called "iron parasitism," wherein iron is scavenged from the local environment using specialized iron chelators called siderophores. C. albicans can steal iron directly from host proteins such as hemoglobin³⁷. Other important minerals directly scavenged by C. albicans include zinc, copper, calcium, potassium, and sodium³⁸.

Invasive candidiasis also entails direct attack and killing of epithelial cells by Candida and this reduces nutrient uptake. Dead or damaged epithelia are unable to carry out their nutrient absorption function. Candidiasis also triggers inflammation of the gut epithelium which in turn reduces the ability of nutrients to cross the epithelial barrier. Other disease states like colitis and Crohn's disease cause inflammation of the gut so this effect, while important, is not specific to Candidiasis³⁹.

HOW CANXIDA REBUILD RBD AIDS IN FASTER RECOVERY

As we've seen, Candida infection leads to the depletion of many important minerals whether by indirect gut inflammation or direct scavenging. These minerals need to be replaced by supplementation to restore full immune function.

Many people with candidiasis don't want to eat certain foods or are unable to. This means that certain vitamins and minerals may be missing from their diet. CanXida Rebuild contains a variety of minerals and vitamins that are essential for immune function, ensuring that all of the nutritional bases are covered.



INGREDIENT BREAKDOWN

Table 1. CanXida RBD Vitamin Ingredients

VITAMINS	FUNCTION
Vitamin A	Promotes T-cell activation in the immune system and promotes antibody production. Vitamin A helps to maintain a strong epithelial tissue barrier function ²³ .
Vitamin C	Promotes the migration of neutrophils and facilitates neutrophil clearance by macrophages after the immune response ²⁹ . Expedites wound healing by promoting the expression of collagen ^{33,34} .
Vitamin D	Plays an essential role in regulating the immune response and preventing autoimmunity from developing. Essential for the uptake of dietary calcium ²⁵ .
Vitamin E	Important for various aspects of T-cell biology including communication between T-cells and antigen-presenting cells. Also regulates important immune signaling molecules ⁴⁰ .
Thiamin	Plays roles in T-cell differentiation ⁴¹ and glucose processing ⁴² .
Riboflavin	Involved in proper macrophage functioning ⁴³ and may also suppress inflammation through the downregulation of immune signaling complexes (inflammasomes) ⁴⁴ .
Niacin	Provides important cofactors for a variety of enzymatic reactions. Niacin is also important for its anti-inflammatory role in cases of metabolic imbalance ⁴⁵ .
Vitamin B6	Important for T-cell activation and cytokine production. Deficiency of vitamin B6 leads to reduced antibody abundance in serum and it also plays a beneficial role during chronic inflammation ¹¹ .
Folate	Important for the proliferation of various immune cells. Folate deficiency leads to reduced T-cell differentiation, reduced maturation of dendritic cells (cells important for capturing pathogens and "teaching" other immune cells to recognize them), and lower cytokine production ⁴⁵ .

INGREDIENT BREAKDOWN

VITAMINS	FUNCTION
Vitamin B12	Important for the proliferation and function of T-cells and natural killer cells (immune cells that kill cells infected with viruses) ⁴⁶ . Vitamin B12 is important for the production of red blood cells.
Biotin	Important for the maturation and activity of a variety of immune cells including natural killer cells and T-cells ⁴⁷ .
Pantothenic Acid	Less studied than other vitamins but may play a role in barrier function and immunity in the gut ⁴⁵ .



Table 2. CanXida RBD Mineral Ingredients

MINERALS	FUNCTION
Choline	An essential component of cell membranes ⁴⁸ and is required for immune cell expansion and signalling ⁴⁹ .
Calcium	Involved in general immune cell physiology such as activation ²⁶ .
Iron	Often depleted after infection, Iron is involved in the activation and function of many immune cells including T-cells, B-cells (antibody-producing), macrophages, neutrophils, and natural killer cells ¹⁹ .
Magnesium	Involved in T-cell activation ⁸ .
Zinc	Important for the growth and function of B-cells and T-cells, zinc is essential for the function of zinc finger proteins which help to mediate the immune response ^{13,50} .
Selenium	Has been shown to expedite T-cell activation, increase T-cell number, and promote cytokine production ⁵¹ .
Copper	Essential mineral for immune function, particularly in B-cells, T-cells, and neutrophils. Copper deficiency leads to increased susceptibility to infection ⁵² .
Manganese	Essential mineral for my enzymatic processes, manganese is important in T-cell and macrophage signaling, and in cytokine production ⁵³ .
Chromium	Plays both stimulatory and modulatory roles in the immune system. Chromium deficiency leads to decreased humoral (antibody) response.
Molybdenum	May play an immunomodulatory role through the regulation of macrophage metabolism⁵⁴.
Potassium	Required for the antimicrobial function of monocytes and macrophages and in cytokine production ⁵⁵ .
Boron	Plays a mixed role in the immune system, Boron may increase the abundance of T-cells ⁵⁶ and be necessary for macrophage activation ⁵⁷ .
Vanadium	Also plays immune stimulation and immunomodulatory activities. Promotes T- and B-cell activation and regulation of cytokine production ⁵⁸ .

CONCLUSION

The GI is the primary site for the absorption of dietary nutrients and is home to a diverse ecosystem of microorganisms collectively known as the gut microbiome. Several factors affect nutrient absorption from the gut including the diversity of the gut microbiome. Overgrowth of opportunistic pathogens from the Candida genus of fungi disrupts nutrient absorption and reduces the abundance of key nutrients in the body.

Invasive Candida reduces nutrient absorption through direct and indirect mechanisms including damage to epithelial cells and direct scavenging of essential minerals. The nutrients whose absorption is perturbed by Candida, such as zinc and vitamin C, are essential for many bodily processes including immune function. Since the immune system is often compromised in individuals with candidiasis, loss of these nutrients can slow recovery and leave the body open to reinfection.

Canxida Rebuild contains twenty-five essential nutrients that provide support to individuals recovering from candidiasis. These individuals may lack certain nutrients because of infection or from a restricted diet. Each of the vitamins and minerals included in Canxida Rebuild are essential for normal physiological function and are very important in the immune system. Canxida Rebuild's twenty-five vitamins and minerals are backed up by both recent and long-standing scientific data. This wealth of evidence means CanXida Rebuild could benefit people suffering from candidiasis, and help to restore nutrient absorption in the gut.

REFERENCES

- 1. Gibson RS. The Role of Diet- and Host-Related Factors in Nutrient Bioavailability and Thus in Nutrient-Based Dietary Requirement Estimates. Food Nutr Bull. 2007;28(1_suppl1):S77-S100. doi:10.1177/15648265070281S108
- 2. Carabotti M, Annibale B, Lahner E. Common Pitfalls in the Management of Patients with Micronutrient Deficiency: Keep in Mind the Stomach. Nutrients. 2021;13(1):208. doi:10.3390/nu13010208
- 3. D'Alessandro C, Benedetti A, Di Paolo A, Giannese D, Cupisti A. Interactions between Food and Drugs, and Nutritional Status in Renal Patients: A Narrative Review. Nutrients. 2022;14(1):212. doi:10.3390/nu14010212
- Woudstra T, Thomson ABR. Nutrient absorption and intestinal adaptation with ageing. Best Pract Res Clin Gastroenterol. 2002;16(1):1-15. doi:10.1053/bega.2001.0262
- 5. Valdes AM, Walter J, Segal E, Spector TD. Role of the gut microbiota in nutrition and health. BMJ. Published online June 13, 2018:k2179. doi:10.1136/bmj.k2179
- 6. Paillaud E, Merlier I, Dupeyron C, Scherman E, Poupon J, Bories PN. Oral candidiasis and nutritional deficiencies in elderly hospitalised patients. Br J Nutr. 2004;92(5):861-867. doi:10.1079/BJN20041264
- 7. Jahnen-Dechent W, Ketteler M. Magnesium basics. Clin Kidney J. 2012;5(Suppl 1):i3-i14. doi:10.1093/ndtplus/sfr163
- 8. Ashique S, Kumar S, Hussain A, et al. A narrative review on the role of magnesium in immune regulation, inflammation, infectious diseases, and cancer. J Health Popul Nutr. 2023;42(1):74. doi:10.1186/s41043-023-00423-0
- 9. Swaminathan R. Magnesium metabolism and its disorders. Clin Biochem Rev. 2003;24(2):47-66.
- 10. Erdman JW, Macdonald IA, Zeisel SH, eds. Present Knowledge in Nutrition. 1st ed. Wiley; 2012. doi:10.1002/9781119946045
- 11. Stach K, Stach W, Augoff K. Vitamin B6 in Health and Disease. Nutrients. 2021;13(9):3229. doi:10.3390/nu13093229
- 12. Duggan C, Gannon J, Walker WA. Protective nutrients and functional foods for the gastrointestinal tract. Am J Clin Nutr. 2002;75(5):789-808. doi:10.1093/ajcn/75.5.789
- 13. Prasad AS. Zinc in human health: effect of zinc on immune cells. Mol Med Camb Mass. 2008;14(5-6):353-357. doi:10.2119/2008-00033.Prasad
- 14. Thakur K, Tomar SK, Singh AK, Mandal S, Arora S. Riboflavin and health: A review of recent human research. Crit Rev Food Sci Nutr. 2017;57(17):3650-3660. doi:10.1080/10408398.2016.1145104
- 15. Mosegaard S, Dipace G, Bross P, Carlsen J, Gregersen N, Olsen RKJ. Riboflavin Deficiency-Implications for General Human Health and Inborn Errors of Metabolism. Int J Mol Sci. 2020;21(11):3847. doi:10.3390/ijms21113847
- 16. Smith LD, Garg U. Disorders of vitamins and cofactors. In: Biomarkers in Inborn Errors of Metabolism. Elsevier; 2017:361-397. doi:10.1016/B978-0-12-802896-4.00011-0
- 17. Piskin E, Cianciosi D, Gulec S, Tomas M, Capanoglu E. Iron Absorption: Factors, Limitations, and Improvement Methods. ACS Omega. 2022;7(24):20441-20456. doi:10.1021/acsomega.2c01833
- Saboor M, Zehra A, Qamar K, Moinuddin null. Disorders associated with malabsorption of iron: A critical review. Pak J Med Sci. 2015;31(6):1549-1553. doi:10.12669/pjms.316.8125
- 19. Ni S, Yuan Y, Kuang Y, Li X. Iron Metabolism and Immune Regulation. Front Immunol. 2022;13:816282. doi:10.3389/fimmu.2022.816282
- 20. Czeizel A, Dudás I, Vereczkey A, Bánhidy F. Folate Deficiency and Folic Acid Supplementation: The Prevention of Neural-Tube Defects and Congenital Heart Defects. Nutrients. 2013;5(11):4760-4775. doi:10.3390/nu5114760
- 21. Visentin M, Diop-Bove N, Zhao R, Goldman ID. The intestinal absorption of folates. Annu Rev Physiol. 2014;76:251-274. doi:10.1146/annurev-physiol-020911-153251
- 22. Courtemanche C, Elson-Schwab I, Mashiyama ST, Kerry N, Ames BN. Folate Deficiency Inhibits the Proliferation of Primary Human CD8+ T Lymphocytes In Vitro. J Immunol. 2004;173(5):3186-3192. doi:10.4049/jimmunol.173.5.3186
- 23. Carazo A, Macáková K, Matoušová K, Krčmová LK, Protti M, Mladěnka P. Vitamin A Update: Forms, Sources, Kinetics, Detection, Function, Deficiency, Therapeutic Use and Toxicity. Nutrients. 2021;13(5):1703. doi:10.3390/nu13051703
- 24. Huang Z, Liu Y, Qi G, Brand D, Zheng SG. Role of Vitamin A in the Immune System. J Clin Med. 2018;7(9):258. doi:10.3390/jcm7090258

- 25. Christakos S, Dhawan P, Porta A, Mady LJ, Seth T. Vitamin D and intestinal calcium absorption. Mol Cell Endocrinol. 2011;347(1-2):25-29. doi:10.1016/j.mce.2011.05.038
- 26. Vig M, Kinet JP. Calcium signaling in immune cells. Nat Immunol. 2009;10(1):21-27. doi:10.1038/ni.f.220
- 27. Monaco S, Jahraus B, Samstag Y, Bading H. Nuclear calcium is required for human T cell activation. J Cell Biol. 2016;215(2):231-243. doi:10.1083/jcb.201602001
- 28. Carr AC, Rowe S. Factors Affecting Vitamin C Status and Prevalence of Deficiency: A Global Health Perspective. Nutrients. 2020;12(7):1963. doi:10.3390/nu12071963
- 29. Carr AC, Maggini S. Vitamin C and Immune Function. Nutrients. 2017;9(11):1211. doi:10.3390/nu9111211
- 30. Netea MG, Joosten LAB, van der Meer JWM, Kullberg BJ, van de Veerdonk FL. Immune defence against Candida fungal infections. Nat Rev Immunol. 2015;15(10):630-642. doi:10.1038/nri3897
- 31. Guo S, DiPietro LA. Factors Affecting Wound Healing. J Dent Res. 2010;89(3):219-229. doi:10.1177/0022034509359125
- 32. McConnell BB, Kim SS, Bialkowska AB, Yu K, Sitaraman SV, Yang VW. Krüppel-like factor 5 protects against dextran sulfate sodium-induced colonic injury in mice by promoting epithelial repair. Gastroenterology. 2011;140(2):540-549.e2. doi:10.1053/j.gastro.2010.10.061
- 33. Bechara N, Flood VM, Gunton JE. A Systematic Review on the Role of Vitamin C in Tissue Healing. Antioxid Basel Switz. 2022;11(8):1605. doi:10.3390/antiox11081605
- 34. Boyera N, Galey I, Bernard BA. Effect of vitamin C and its derivatives on collagen synthesis and cross-linking by normal human fibroblasts. Int J Cosmet Sci. 1998;20(3):151-158. doi:10.1046/j.1467-2494.1998.171747.x
- 35. Geesin JC, Darr D, Kaufman R, Murad S, Pinnell SR. Ascorbic acid specifically increases type I and type III procollagen messenger RNA levels in human skin fibroblast. J Invest Dermatol. 1988;90(4):420-424. doi:10.1111/1523-1747.ep12460849
- 36. Tucey TM, Verma J, Harrison PF, et al. Glucose Homeostasis Is Important for Immune Cell Viability during Candida Challenge and Host Survival of Systemic Fungal Infection. Cell Metab. 2018;27(5):988-1006.e7. doi:10.1016/j.cmet.2018.03.019
- 37. Almeida RS, Wilson D, Hube B. Candida albicans iron acquisition within the host. FEMS Yeast Res. 2009;9(7):1000-1012. doi:10.1111/j.1567-1364.2009.00570.x
- 38. Volkova M, Atamas A, Tsarenko A, Rogachev A, Guskov A. Cation Transporters of Candida albicans-New Targets to Fight Candidiasis? Biomolecules. 2021;11(4):584. doi:10.3390/biom11040584
- 39. Farré R, Fiorani M, Abdu Rahiman S, Matteoli G. Intestinal Permeability, Inflammation and the Role of Nutrients. Nutrients. 2020;12(4):1185. doi:10.3390/nu12041185
- 40. Lewis ED, Meydani SN, Wu D. Regulatory role of vitamin E in the immune system and inflammation. IUBMB Life. 2019;71(4):487-494. doi:10.1002/iub.1976
- 41. Hirata SI, Sawane K, Adachi J, et al. Vitamin B1 Supports the Differentiation of T Cells through TGF-β Superfamily Production in Thymic Stromal Cells. iScience. 2020;23(9):101426. doi:10.1016/j.isci.2020.101426
- 42. Lonsdale D. A review of the biochemistry, metabolism and clinical benefits of thiamin(e) and its derivatives. Evid-Based Complement Altern Med ECAM. 2006;3(1):49-59. doi:10.1093/ecam/nek009
- Mazur-Bialy AI, Pochec E, Plytycz B. Immunomodulatory effect of riboflavin deficiency and enrichment reversible pathological response versus silencing of inflammatory activation. J Physiol Pharmacol Off J Pol Physiol Soc. 2015;66(6):793-802.
- 44. Ahn H, Lee GS. Riboflavin, vitamin B2, attenuates NLRP3, NLRC4, AIM2, and non-canonical inflammasomes by the inhibition of caspase-1 activity. Sci Rep. 2020;10(1):19091. doi:10.1038/s41598-020-76251-7
- 45. Peterson CT, Rodionov DA, Osterman AL, Peterson SN. B Vitamins and Their Role in Immune Regulation and Cancer. Nutrients. 2020;12(11):3380. doi:10.3390/nu12113380
- Tamura J, Kubota K, Murakami H, et al. Immunomodulation by vitamin B12: augmentation of CD8+ T lymphocytes and natural killer (NK) cell activity in vitamin B12-deficient patients by methyl-B12 treatment. Clin Exp Immunol. 2001;116(1):28-32. doi:10.1046/j.1365-2249.1999.00870.

- 49. Hubler MJ, Kennedy AJ. Role of lipids in the metabolism and activation of immune cells. J Nutr Biochem. 2016;34:1-7. doi:10.1016/j.jnutbio.2015.11.002
- 50. Rakhra G, Rakhra G. Zinc finger proteins: insights into the transcriptional and post transcriptional regulation of immune response. Mol Biol Rep. 2021;48(7):5735-5743. doi:10.1007/s11033-021-06556-x
- 51. Broome CS, McArdle F, Kyle JA, et al. An increase in selenium intake improves immune function and poliovirus handling in adults with marginal selenium status. Am J Clin Nutr. 2004;80(1):154-162. doi:10.1093/ajcn/80.1.154
- 52. Cheng F, Peng G, Lu Y, et al. Relationship between copper and immunity: The potential role of copper in tumor immunity. Front Oncol. 2022;12:1019153. doi:10.3389/fonc.2022.1019153
- 53. Wu Q, Mu Q, Xia Z, Min J, Wang F. Manganese homeostasis at the host-pathogen interface and in the host immune system. Semin Cell Dev Biol. 2021;115:45-53. doi:10.1016/j.semcdb.2020.12.006
- 54. He XT, Li X, Zhang M, et al. Role of molybdenum in material immunomodulation and periodontal wound healing: Targeting immunometabolism and mitochondrial function for macrophage modulation. Biomaterials. 2022;283:121439. doi:10.1016/j.biomaterials.2022.121439
- 55. Do EA, Gries CM. Beyond Homeostasis: Potassium and Pathogenesis during Bacterial Infections. Infect Immun. 2021;89(7):e0076620. doi:10.1128/IAI.00766-20
- 56. Arciniega-Martínez IM, Romero-Aguilar KS, Farfán-García ED, García-Machorro J, Reséndiz-Albor AA, Soriano-Ursúa MA. Diversity of effects induced by boron-containing compounds on immune response cells and on antibodies in basal state. J Trace Elem Med Biol. 2022;69:126901. doi:10.1016/j.jtemb.2021.126901
- 57. Routray I, Ali S. Boron Induces Lymphocyte Proliferation and Modulates the Priming Effects of Lipopolysaccharide on Macrophages. Mattei F, ed. PLOS ONE. 2016;11(3):e0150607. doi:10.1371/journal.pone.0150607
- 58. Tsave O, Petanidis S, Kioseoglou E, et al. Role of Vanadium in Cellular and Molecular Immunology: Association with I mmune-Related Inflammation and Pharmacotoxicology Mechanisms. Oxid Med Cell Longev. 2016;2016:4013639. doi:10.1155/2016/4013639