

References

1. Role of Vitamin A in the Immune System, Zhiyi Huang, Yu Liu, Guangying Qi, David Brand, Song Guo Zheng. *J Clin Med*. 2018 Sep 6;7(9):258.
2. Vitamin effects on the immune system: vitamins A and D take centre stage. Mora JR, Iwata M, von Andrian UH. *Nat Rev Immunol*. 2008;8(9):685-698. doi:10.1038/nri2378
3. Retinoic acid modulates interferon- γ production by hepatic killer T cells via phosphatase 2A and the extracellular signal-regulated kinase pathway. Heng-Kwei Chang, Wu-Shiun Hou. *J Interferon Cytokine Res*. 2015 Mar;35(3):200-12.
4. Immune-Boosting role of vitamins D, C, E, zinc, selenium and omega-3 fatty acids: Could they help against Covid-19? Hira Shakoor, Jack Feehan, Ayesha S. Al Dhaheri, Habiba I. Ali, Carine Platat, Leila Cheikh Ismail, Vasso Apostolopoulos and Lily Stojanovska. *Maturitas*. 2021 Jan;143:1-9.
5. Huijckens M et al. *Cytotherapy*. 2015;17(5):613-620.
6. Vitamin C and Immune Function. Antira C Car, Silvia Maggini, *Nutrients*. 2017 Nov 3;9(11):1211.
7. Vitamin D and Immune function. Prietl, B., Treiber, G., Piber, T. R. & Amrein, K. *Nutrients*. 5, 2502–2521 (2013).
8. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. Martineau, A. R. *BMJ* 356, 6583–6594 (2017).
9. A review of micronutrients and the immune system-working in harmony to reduce the risk of infection. Gombart, A. F., Pierre, A. & Maggini, S. *Nutrients*. 12(1), 236.
10. *Cathelins (Innate Immunity) Physiology of the Gastrointestinal Tract (Fourth Edition)* by Lars Eckmann, 2006.
11. Vitamin D supplementation of initially vitamin D-deficient mice diminishes lung inflammation with limited effects on pulmonary epithelial integrity. Shelley Gorman, Alysia G Buckley, Kak-Ming Ling, Luke J Berry, Vanessa S Fear, Stephen M Stick, Alexander N Larcombe, Anthony Kicic, Prue H Hart, *Physiol Rep*. 2017 Aug;5(15):e13371.
12. Latitude Dependence of the COVID-19 Mortality Rate – A Possible Relationship to Vitamin D Deficiency? Mark Braiman, Syracuse University Department of Chemistry. 25 Jun 2020.
13. Alterations in the expression of inflammatory parameters as a result of oxidative stress produced by moderate zinc deficiency in rat lung. Verónica S. Biaggio, María V. Pérez Chaca, Susana R. Valdéz, Nidia N. Gómez and María S. Gimenez. *Experimental Lung Research*, Volume 36, 2010 – Issue 1.
14. Zinc and respiratory tract infections: Perspectives for COVID-19 (Review). Anatoly V Skalny, Lothar Rink, Olga P Ajsuvakova, Michael Aschner, Viktor A Gritsenko, Svetlana I Alekseenko, Andrey A Svistunov, Demetrios Petrakis, Demetrios A Spandidos, Jan Aaseth, Aristidis Tsatsakis, Alexey A Tinkov. *Int J Mol Med*. 2020 July;46(1):17-26.
15. COVID-19 Pandemic: Can Maintaining Optimal Zinc Balance Enhance Host Resistance? Mohammed S Razaque, Tohoku J Exp Med. 2020 July;251(3):175-181.
16. Association between regional selenium status and reported outcome of COVID-19 cases in China. Jinsong Zhang, Ethan Will Taylor, Kate Bennett, Ramy Saad, Margaret P Rayman. *Am J Clin Nutr*. 2020 Jun 1;111(5):1297-1299.
17. Host nutritional selenium status as a driving force for influenza virus mutations. HK Nelson, Q Shi, P Van Dael, EJ Schiffrin, S Blum, D Barclay, OA Levander, MA Beck. *FASEB J*. 2001 Aug;15(10):1727-1738.
18. The influence of selenium on immune responses. Peter R Hoffmann and Maria J. Berry. *Mol Nutr Food Res*. 2008 Nov;51(11):1273-1280.
19. Zhongcheng Shi and Carlos A Puyo. N-Acetylcysteine to Combat COVID-19: An Evidence Review. *Ther Clin Risk Manag*. 2020;16:1047-1055.
20. S De Flora, C Grassi, L Carati. Attenuation of influenza-like symptomatology and improvement of cell-mediated immunity with long-term N-acetylcysteine treatment. *Eur Respir J*. 1997 Jul;10(7):1535-41.
21. Silvio De Flora, Roumen Balansky, Sebastiano La Maestra. Rationale for the use of N-acetylcysteine in both prevention and adjuvant therapy of COVID-10. *The FASEB Journal*/Volume 34, Issue 10.
22. Aikaterini Nasi, Stephanie McArdle, Gustav Gaudernack, Gabriel Westman, Cornelis Mielief, Johan Rockberg, Ramon Arens, Demetrios Kouretas, Jan Sjölin, Sara Mangsbo. Reactive oxygen species as an initiator of toxic innate immune response in retort to SARS-CoV-2 in an aging population, consider N-acetylcysteine as early therapeutic intervention. *Toxicol Rep*. 202 Jun 18;7:768-771.
23. Memorial Sloan Kettering Cancer Center. A Study of N-acetylcysteine in Patients with COVID-19 Infection. US National Library of Medicine. [ClinicalTrials.gov Identifier: NCT04374461](https://clinicaltrials.gov/ct2/show/study/NCT04374461). Updated post: November 27, 2020.
24. Christian Krawitz, Mobarak Abu Mraheil, Michael Stein, Can Imrizlioglu, Eugen Domann, Stephan Pleschka and Torsten Hain. Inhibitory activity of a standardized elderberry liquid extract against clinically-relevant human respiratory bacterial pathogens and influenza A and B viruses. *BMC Complement Altern Med*. 2011;11:16.
25. Julia Wermig-Morgan. Elderberry is anti-bacterial, anti-viral and modulates the immune system: anti-bacterial, anti-viral and immunomodulatory non-clinical (in-vitro) effects of elderberry fruits and flowers (Sambucus nigra): a systematic review. *Research Gate*. November 2020. Thesis for MSc in Evidence-Based Health Medicine, University of Oxford.
26. Christie Chen, David M Zuckerman, Susanna Brantley, Michka Sharpe, Kevin Childress, Egbert Hoiczky and Amanda R Pendleton. *Sambucus nigra* extracts inhibit infectious bronchitis virus at an early point during replication. *BMC Vet Res*. 2014;10:24.

27. Ali Salehzadeh, Leila Asadpour, Akram Sadat Naeemi and Elham Houshmand. Antimicrobial Activity of Methanolic Extracts of *Sambucus Ebulus* and *Urtica Dioica* Against Clinical Isolates of Methicillin Resistant *Staphylococcus Aureus*. *Afr J Tradit Complement Altern Med*. 2014;11(5):38-40.
28. Marta Menegazzi, Rachele Campagnari, Mariarita Bertoldi, Rosalia Crupi, Rosanna Di Paola and Salvatore Cuzzocrea. Protective Effect of Epigallocatechin-3-Gallate (EGCG) in Diseases with Uncontrolled Immune Activation: Could Such a Scenario Be Helpful to Counteract COVID-19? *Int J Mol Sci*. 2020Jul;21(14):5171.
29. Narayanan Sriram, Srinivasan Kalayarasan, Ganapasam Sudhandiran. Epigallocatechin-3-gallate augments antioxidant activities and inhibits inflammation during bleomycin-induced experimental pulmonary fibrosis through Nrf2-Keap1 signaling. *Pul Pharmacol Ther*. 2009 Jun;22(3):221-36.
30. Kunihiko Kaihatsu, Miyuki Yamabe, Yasuhito Ebara. Antiviral Mechanism of Action of Epigallocatechin-3-O-gallate and Its Fatty Acid Esters. *Molecules*. 2018 Sep 27;23(10):2475.
31. Wei Li, Mala Ashok, Jianhua Li, Huan Yang, Andrew E Sama, Haichao Wang. A major ingredient of green tea rescues mice from lethal sepsis partly by inhibiting HMGB1. *PLoS One*. 2007 Nov 7;2(11):e1153.
32. Narayanan Sriram, Srinivasan Kalayarasan, Ganapasam Sudhandiran. Epigallocatechin-3-gallate exhibits anti-fibrotic effect by attenuating bleomycin-induced glycoconjugates, lysosomal hydrolases and ultrastructural changes in rat model pulmonary fibrosis. *Chem Biol Interact*. 2009 Jul 15;180(2):271-80.
33. Stephen Hsu. Compounds Derived from Epigallocatechin-3-Gallate (EGCG) as a Novel Approach to the Prevention of Viral Infections. *Inflamm Allergy Drug Targets*. 2015;14(1):13-8.
34. Ulf Andersson, William Ottestad, Kevin J Tracey. Extracellular HMGB1: a therapeutic target in severe pulmonary inflammation including COVID-19? *Mol Med*. 2020 May 7:26(1):42.
35. Tina M. St. Jhn MD. *Astragalus*. *Integrative Medicine (Fourth Edition)*, 2018.
36. Daniel J Morena Fernández-Ayala, Plácido Navas, Guillermo López-Lluch. Age-related mitochondrial dysfunction as a key factor in COVID-19 disease. *Exp Gerontol*. 2020 Dec;142:111147.
37. Lorenzo Galluzzi, Oliver Kepp, Christina Trojel-Hansen, Guido Kroemer. Mitochondrial control of cellular life, stress, and death. *Circ Res*. 2012 Oct 12;111(9):1198-207.
38. Pawan K Agrawal, Chandan Agrawal, Gerald Blunden. Quercetin: Antiviral Significance and Possible COVID-19 Integrative Considerations. *Sage Journals*. December 3, 2020.
39. Ruben Manuel Luciano Colunga Biancatelli, Max Berrill, John D. Catravas, Paul E. Marik. Quercetin and Vitamin C: An Experimental, Synergistic Therapy for the Prevention and Treatment of SARS-CoV-2 Related Disease (COVID-19). *Front Immunol*. 2020;11:1451.
40. Effect of quercetin supplementation on plasma lipid profiles, blood pressure and glucose levels: a systematic review and meta-analysis. Dodd S et al. *Expert Opin Biol Ther*. 2008;8(12):1955-1962.
41. Noboru Uchida, Hiroo Toyoda. Antioxidant therapy as a potential approach to several influenza-associated complications. *Molecules*. 2011 Feb 28;16(3):2032-52.

Additional references:

1. Bishop E, Ismailova A, Dimeloe SK, Hewison M, White JH. 2020 Vitamin D and immune regulation: antibacterial, antiviral, anti-inflammatory. *JBM R Plus* e10405.
2. Christakos S et al. 2013 Vitamin D: beyond bone. *An. N.Y. Acad. Sci.* 1287, 45-58.
3. Jan Alexander, Alexey Tinkov, Tor A Strand, Urban Alehagen, Anatoly Skalny, Jan Aaseth. Early Nutritional Interventions with Zinc, Selenium and Vitamin D for Raising Anti-Viral Resistance Against Progressive COVID-19. *Nutrients*. 2020 Aug 7;12(8):2358.
4. Laird, E., Rhodes, J. & Kenny, R. A. Vitamin D and inflammation: potential implications for severity of covid-19. *Ir. Med. J.* 113(5), 81 (2020).
5. Prasad AS et al. *Am J Clin Nutr*. 2007;85:837-844.
6. Kerkick C, Willoughby DJ. *Int Soc Sports Nutr*. 2005 Dec 9;2(2):38-44. doi: 10.1186/1550-2783-2-2-38.
7. De Flora S, Grassi C, Carati L. *Eur Respir J*. 1997 Jul;10(7):1535-41. doi: 10.1183/09031936.97.10071535.
8. The effect of oral N-acetylcysteine in chronic bronchitis: a quantitative systematic review. Wei J et al. *Adv Ther*. 2019;36(12):3356-3367.
9. Evlambia Harokopakis 1, Mohamad H Albzreh, Elaine M Haase, Frank A Scannapieco, George Hajishengallis. Inhibition of proinflammatory activities of major periodontal pathogens by aqueous extracts from elder flower (*Sambucus nigra*) *J Periodontol*. 2006 Feb;77(2):271-9. doi: 10.1902/jop.2006.050232.
10. Anti-infective properties of epigallocatechin-3-gallate (EGCG), a component of green tea. Steinmann J et al. *Br J Pharmacol*. 2013; 168(5): 1059–1073.

Immune Support Packs

- Supports a healthy immune response*
- Protects against oxidative stress*
- Supports cardiovascular health*
- Promotes a balanced inflammatory response*

Biotics Research **Immune Support Packs** contain a carefully selected and comprehensive array of nutrients designed to support the body's overall healthy immune response. Each packet includes the most powerful immune-supportive ingredients from top-selling Biotics Research's products such as vitamins A, C and D, zinc, selenium, NAC, CoQ10, curcumin and manganese, all in clinically relevant amounts.

In addition, this potent formula includes elderberry and green tea extracts, astragalus, quercetin and citrus bioflavonoids for additional immune and antioxidant support.

Immune health does not exist in a bubble, but rather is supported or undermined by various lifestyle factors such as sleep, stress, diet, digestive health and age. **Immune Support Packs** provide nutrients shown to support multiple physiological pathways that bolster overall immunity.

Vitamin A (750 mcgRAE) (2,500 IU)

Vitamin A is involved in the development of the immune system and plays regulatory roles in cellular immune responses and humoral immune processes.¹ It also plays an essential role in a large number of physiological functions that encompass vision, growth, reproduction and immunity. Vitamin A has a crucial effect on the immune response, with its metabolite retinoic acid having hormone-like properties that exert effect by binding to nuclear-hormone receptors. Retinoic acid enhances cytotoxicity and T-cell proliferation.²



The immune organs where most immunocompetent cells proliferate, differentiate, mature, aggregate and respond to immunity need a constant dietary intake to maintain their vitamin A concentrations. Vitamin A is particularly important for the effective function of the innate immune system, which is a broad type of protection already present in the body.

Vitamin C (1,000 mg)

A strong antioxidant used to boost blood antioxidant levels, vitamin C helps support the body's natural defense mechanisms and a healthy inflammation response. Vitamin C works very well on its own as well as in combination with other immune boosters. In a recent review, its immunomodulatory actions included acting as a free radical fighter and protecting biomolecules such as proteins, lipids and nucleotides from oxidative damage and dysfunction. It also plays a role in supporting normal respiratory defense mechanisms and working as a natural antihistamine.⁴ Vitamin C has also been found useful for regulating cytokines that may occur in certain respiratory situations.⁴ Ascorbic acid also promotes proliferation of natural killer cell populations in culture systems.⁵



(800) 231-5777

6801 Biotics Research Drive • Rosenberg, TX 77471
biotics@bioticsresearch.com • www.bioticsresearch.com

*These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.

© 2021 Biotics Research Corp., Rosenberg, TX 77471
LIT-338 Rev. 09/21



(800) 231-5777

6801 Biotics Research Drive • Rosenberg, TX 77471
biotics@bioticsresearch.com • www.bioticsresearch.com

*These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.

© 2021 Biotics Research Corp., Rosenberg, TX 77471
LIT-338 Rev. 09/21

The role of vitamin C in lymphocyte function is not yet clear, but it has been seen to support the normal differentiation and proliferation of B- and T-cells, potentially thanks to its gene-regulating effect.⁶ Infections significantly impact vitamin C levels due to enhanced inflammation and metabolic requirements, and since deficiency can lead to impaired immunity and higher susceptibility to infections, vitamin C supplementation may be a great ally to optimize cell and tissue levels.

Vitamin D (100 mcg) (4,000 IU)

Vitamin D is best known for its role in the maintenance of bone health and calcium–phosphorus metabolism, but many other roles like stimulation of insulin production, effects on myocardial contractility and its essential role in immune function have been recently discovered. Vitamin D plays an essential role in the immune system by interfering with the majority of the immune cells such as macrophages, B and T lymphocytes, neutrophils and dendritic cells.⁷ The T and B lymphocytes can form the active metabolite of vitamin D, 1,25(OH)2D3, which inhibits T cell proliferation and activation. In addition, vitamin D inhibits the production of pro-inflammatory cytokines and enhances the production of anti-inflammatory cytokines.^{8,9}

Vitamin D's effect on innate and adaptive immune response has been extensively analyzed in recent years. It enhances innate cellular immunity through the stimulation of expression of antimicrobial peptides such as cathelicidin and defensins. Cathelicidin is capable of influencing the activity of viruses, bacteria and fungi.¹⁰ Defensins maintain tight and gap junctions and enhance the expression of anti-oxidative genes. This is important because risk of infection and pulmonary edema increase when the integrity of epithelial tight junctions is damaged.⁴ Vitamin D helps to maintain the integrity of epithelial tight junctions.¹¹

Vitamin D provides extensive immune support. It promotes the differentiation of monocytes to macrophages, while increasing phagocytosis and pathogen elimination. It modulates the adaptive immune response by suppressing T helper type-1 cell function and influencing the production of pro-inflammatory cytokines IL-2 and interferon-gamma. This work is particularly key for communities living in the northern hemisphere, where there are higher rates of vitamin D deficiency from a lack of sufficient sunshine.¹²

Zinc (25 mg)

Zinc is vital for both the innate and acquired immune responses. Deficiency markedly increases pro-inflammatory cytokines and the unhealthy remodeling of lung tissue in animals.¹³ However, what really makes zinc stand out is its immunomodulatory properties.^{14,15} Zinc has positive effects on NK cells, phagocytosis, the generation of oxidative burst, and T cells. Zinc helps to

increase the number of T cells, especially in the elderly, as this population is often deficient in this mineral.

Selenium (70 mcg)

Selenium has gained considerable attention with recent studies highlighting selenium deficiency and its correlation to infection.¹⁶ Selenium and vitamin E both act on antioxidant pathways to increase the number of T cells at work in the body to enhance mitogenesis, lymphocyte responses and NK cell activity, and increase IL-2 cytokine secretion.⁴ Many animal studies on selenium published recently show selenium's effect to foster cell-mediated immunity and selenium status could affect viral activity.¹⁷ Selenium is thought to work on cell-mediated immunity rather than humoral immunity, but is considered important in supporting an overall healthy immune response.¹⁸

Manganese (2 mg)

Although the body only requires small amounts of manganese, it is essential for the normal function of the brain, nervous system and many of the body's enzyme systems.

Copper (0.75 mg)

Copper plays an important role in the production of red blood cells, regulation of heart rate and blood pressure, absorption of iron, prostate health, immune system activation and the healthy development of bone, connective tissue and organs such as the brain and heart.

NAC (1,000 mg)

N-acetylcysteine (NAC) is a precursor to the antioxidant glutathione. NAC has been used to loosen thick mucus in the lungs for decades, but it is also helpful for boosting the immune system via improved cell-mediated immunity, inflammation regulation and antioxidant strength.^{19,20,21} These benefits have been supported recently by small trials and interventions with many scheduled to provide further data on the benefits of oral and intravenous NAC supplementation in immunity.^{22,23}

Elderberry (250 mg)

Elderberry (*Sambucus nigra*) is another immune-supportive star that has risen in recent years, with research focusing on its immunomodulatory effects.²⁴ A recent review demonstrated that elderberry extract from fruit and flowers appears to show inhibitory effects against many pathogenic microorganisms.^{25, 26, 27} Case studies also show that elderberry has potential as an ingredient in a hospital disinfectant, and species of *Sambucus* appear to have very similar antibacterial properties.²⁵

Green Tea (50% EGCG) (200mg)

Epigallocatechin-3-gallate, or EGCG, is being researched in its role to support the immune system, as it may help support healthy cytokine production.²⁸ EGCG is the most abundant component in green tea leaves and is a well-known antioxidant and fighter of free radicals.²⁹ In addition to antiviral³⁰ and anti-sepsis³¹ actions, the main benefit of EGCG lies in its ability to support healthy tissues³² and the ability to simultaneously downregulate expression and signaling of inflammatory mediators, as well as to restore the natural immunological homeostasis where imbalance may be found.^{33,34,28}

Astragalus (200 mg)

Astragalus has been widely used in traditional Chinese medicine. It was shown to have immunostimulatory effects and has been used to support patients with a wealth of health issues.³⁵ Immunomodulation is the purported mechanism of action, with enhanced immunoglobulin production and the restoration of lost T-cell activity among the significant actions.

Coenzyme Q10 (50 mg)

Coenzyme Q10 (CoQ10) is a compound stored in the mitochondria that helps generate energy in cells. The mitochondria are the powerhouse of the cell. Because the strength of the immune system is linked to the health of the mitochondria, a deficiency of CoQ10 can affect the immune system. Certain viral infections affect elderly people and those with comorbidities such as metabolic syndrome, obesity, type 2 diabetes, lung and cardiovascular diseases. Because mitochondrial dysfunction is one of the hallmarks of aging and viral risk factors, fostering mitochondrial turnover, dynamics and activity may support those at risk.³⁶ CoQ10 also acts as an antioxidant, neutralizing free radicals and protecting cells from oxidative damage.³⁷

Quercetin (50 mg)

Another effective immunomodulator worth mention is quercetin, a dietary flavonoid that has been heralded as a potent aid for the current immunological climate.³⁸ That is due to a well-known experimental approach using vitamin C and quercetin together.³⁹ Alongside vitamin C, quercetin is thought to provide free-radical fighting and immunomodulatory effects. Not only does quercetin promote a healthy immune response; it also supports cardiovascular health by maintaining healthy blood pressure levels already in the normal range, promoting healthy HDL function, and supporting endothelial health.^{40,41}



Immune Support Packs are available in a 30 pack bottle (#8141).

Recommended Use: As a dietary supplement, take one packet per day, or as directed by your healthcare practitioner.

Supplement Facts		
Serving Size: 1 Pack Servings per Container: 30		
	Amount Per Serving	% Daily Value
Vitamin A (as acetate)	750 mcgRAE (2,500 IU)	83%
Vitamin C (as ascorbic acid and calcium ascorbate)	1,000 mg	1,111%
Vitamin D (as D ₃ cholecalciferol)	100 mcg (4,000 IU)	500%
Zinc (as zinc gluconate and citrate)	25 mg	227%
Selenium (as raw vegetable culture and selenomethionine)	70 mcg	127%
Manganese (as manganese gluconate)	2 mg	87%
Copper (as copper gluconate)	0.75 mg	83%
NAC (N-Acetyl-L-Cysteine)	1,000 mg	*
Elderberry (Sambucus nigra)(fruit)(extract)	250 mg	*
Green Tea (50% EGCG)	200 mg	*
Astragalus (Astragalus membranaceous)(root)(extract)	200 mg	*
Coenzyme Q10 (emulsified)	50 mg	*
Quercetin	50 mg	*
Citrus bioflavonoids	50 mg	*
Phytolens (Lens esculenta)(husk)(extract)	5 mg	*
*Daily Value not established		
Other Ingredients: Capsule shell (gelatin and water) and magnesium stearate (vegetable source).		
This product is gluten free.		
CAUTION: Not recommended for pregnant or lactating women.		
RECOMMENDATION: One (1) pack each day as a dietary supplement or as otherwise directed by a healthcare professional.		
KEEP OUT OF REACH OF CHILDREN Store in a cool, dry area. Sealed with an imprinted safety seal for your protection.		
Product # 8141 Rev. 08/21		

*These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.