

PRO IMMUNE GOLD

EMPOWERING YOUR IMMUNE RESPONSE



CELLULAR
CYCLICAL
COMPREHENSIVE



A patented comprehensive protocol that improves immune response by improving cellular environment with clinically proven and published Immune boosters, Antioxidants, Anti-inflammatory, Vitamins, Minerals and Nutrients.

NATURAL PROTECTION, PREVENTION AND AMELIORATION OF COVID-19

Colostrum

Colostrum has immune-boosting effects from Magnesium, B vitamins, and vitamins A, C, and E, growth factors IGF-1, IGF-2. Immunoglobulins, IgA, IgG, & IgM provide ready to use passive immunity against respiratory and enteric viral infections.

1. McGrath BA, et al. Composition and properties of bovine colostrum: a review. *Dairy Sci. & Technol.* (2016) 96: 133.
2. Ulfman LH, et al. Effects of Bovine Immunoglobulins on Immune Function, Allergy, and Infection. *Front Nutr.* 2018;5:52.
3. Hurley WL, Theil PK. Perspectives on immunoglobulins in colostrum and milk. *Nutrients.* 2011;3(4):442-474. doi:10.3390/nu3040442.
4. Stelwagen K, et al. Immune components of bovine colostrum and milk. *J Anim Sci.* 2009 Apr;87(13 Suppl):3-9. doi: 10.2527/jas.2008-1377. Epub 2008 Oct 24. PMID: 18952725.

Lactoferrin

Lactoferrin binds to the Heparan sulfate proteoglycans (HSPGs) have been identified as initial adhesion molecules thus preventing viral entry into the cells. Lactoferrin also binds directly to virus diverting them away from the target cells.

Lactoferrin is anti-inflammatory, immunomodulatory moderates the host response to infections and has the dual ability to stimulate the immune system as well as prevent harmful host immune and inflammatory response.

Lactoferrin regulates iron metabolism and prevents replication of the virus to reduce the viral load helping in prevention, control of infection and early recovery.

1. Lang J, et. al. (2011) Inhibition of SARS Pseudovirus Cell Entry by Lactoferrin Binding to Heparan Sulfate Proteoglycans. *PLoS ONE* 6(8): e23710. doi:10.1371/journal.pone.0023710
2. Chang R, Ng TB, Sun WZ. Lactoferrin as potential preventative and adjunct treatment for COVID-19. *Int J Antimicrob Agents.* 2020;56(3):106118. doi:10.1016/j.ijantimicag.2020.106118.

Seaweed

Throughout human history, seaweeds have been used as food, folk remedies, nutraceuticals, functional foods with dietary benefits much beyond their macronutrient content.

Seaweeds offers multiple beneficial compounds, ACE inhibitor peptides, omega-3, fucoxanthin, fucosterol, vitamin D3, B12, phlorotannins and soluble dietary fiber. The delivering antioxidant, anti-inflammatory, and antiviral effects. ACE inhibition directly prevents the mechanism of SARS-CoV-2 infection.

Seaweed components are selective inhibitors of cathepsin L, the lysosomal cysteine protease utilized by corona viruses to release RNA material inside the cells. Thus inhibiting SARS-CoV-2 infection.

1. Emer Shannon & Nissreen Abu-Ghannam (2019) Seaweeds as nutraceuticals for health and nutrition , *Phycologia*, 58:5, 563-577, DOI: 10.1080/00318884.2019.1640533.
2. Tamama K. Potential benefits of dietary seaweeds as protection against COVID-19. *Nutr Rev.* 2020 Dec 20:nuaa126. doi: 10.1093/nutrit/nuaa126.
3. Taghialatela-Scafati, O. New Hopes for Drugs against COVID-19 Come from the Sea. *Mar. Drugs* 2021, 19, 104. <https://doi.org/10.3390/md19020104>.

Role of Curcumin in preventing Covid-19

Curcumin is antiviral, antinociceptive, anti-inflammatory, antipyretic, and antifatigue effects that could be effective to manage the symptoms of the infected patient with COVID-19.

Curcumin exerts antiviral activity against many types of enveloped viruses,

including SARS-CoV-2, by multiple mechanisms: direct interaction with viral membrane proteins; disruption of the viral envelope; inhibition of viral proteases and inducing host antiviral response.

Curcumin protects from pneumonia and ARDS by action against NF- κ B, inflammasome, IL-6 trans signal, and HMGB1 pathways.

Curcumin has demonstrated dual binding affinity to both the viral S protein and the ACE2 receptors on the cells, thus antagonizing the entry of SARS-CoV2 into the cells and preventing infection.

Curcumin achieves significant decrease in proinflammatory cytokines TNF- α , IL-6 and reactive oxygen species, preventing and protecting against Covid 19 infection. It has effects on Toll-like receptors, NF- κ B, inflammatory cytokines, chemokines, and bradykinin making it a choice in the prevention and management of Covid 19

1. Thimmulappa RK, et.al. Antiviral and immunomodulatory activity of curcumin: A case for prophylactic therapy for COVID-19. *Heliyon*. 2021 Feb;7(2):e06350. doi: 10.1016/j.heliyon.2021.e06350.
2. Das S, et.al. An investigation into the identification of potential inhibitors of SARS-CoV-2 main protease using molecular docking study. *J Biomol Struct Dyn*. 2020 May 13:1-11. doi: 10.1080/07391102.2020.1763201.
3. Li HY, et.al. Curcumin inhibits angiotensin II-induced inflammation and proliferation of rat vascular smooth muscle cells by elevating PPAR- γ activity and reducing oxidative stress. *Int J Mol Med*. 2017 May;39(5):1307-1316. doi: 10.3892/ijmm.2017.2924.
4. Babaei F, et.al. Curcumin (a constituent of turmeric): New treatment option against COVID-19. *Food Sci Nutr*. 2020 Sep 6;8(10):5215-5227. doi: 10.1002/fsn3.1858.

Vitamin D in Covid:

COVID-19 is characterized by rise in IL-6 and IL-1, macrophage activation and "cytokine storm", dysregulating the innate immunity. Vitamin D receptors (VDR) regulate, innate and adaptive immune responses, inhibiting cytokine release. Vitamin D suppresses key pro-inflammatory pathways, nuclear factor kappa B (NF- κ B), interleukin-6 (IL-6), and tumor necrosis factor (TNF).

Vitamin D might prevent loss of neural sensation in COVID-19 by stimulating expression of neurotrophins like Nerve Growth Factor (NGF):
Vitamin D: Induction of key neurotrophic factors.

A significant negative correlation ($p=0.033$) has been observed between mean vitamin D levels and COVID-19 cases per one million population in European countries.

Vitamin D receptors (VDR) are highly-expressed in B-lymphocytes, T-lymphocytes, monocytes & macrophages, modulates both innate and adaptive immunity & downregulates inflammation.

Vit D deficient patients have higher incidence of Covid infection and risk of severe disease

1. Malaguarnera L. Vitamin D3 as Potential Treatment Adjuncts for COVID-19. *Nutrients*. 2020 Nov 14;12(11):3512. doi: 10.3390/nu12113512.
2. Xu Y, Baylink DJ, et.al. The importance of vitamin d metabolism as a potential prophylactic, immunoregulatory and neuroprotective treatment for COVID-19. *J Transl Med*. 2020 Aug 26;18(1):322. doi: 10.1186/s12967-020-02488-5.
3. Ali N. Role of vitamin D in preventing of COVID-19 infection, progression and severity. *J Infect Public Health*. 2020 Oct;13(10):1373-1380. doi: 10.1016/j.jiph.2020.06.021.
4. Cutolo M, Paolino S, Smith V. Evidences for a protective role of vitamin D in COVID-19 RMD Open 2020;6:e001454. doi: 10.1136/rmdopen-2020-001454.
5. Rastogi A, et al. Short term, high-dose vitamin D supplementation for COVID-19 disease: a randomised, placebo-controlled, study (SHADE study). *Postgraduate Medical Journal Published Online First: 12 November 2020*. doi: 10.1136/postgradmedj-2020-139065

N Acetyl Cysteine:

NAC inhibit fibrous exudation in interstitial lung disease, decreases TNF- α , IL-1 β , IL-6, IL-8, IL-10, and IL-17 serum levels in patients with sepsis, reduce cytokine storm.

1. De Flora, S, Balansky, R, La Maestra, S. Rationale for the use of N-acetylcysteine in both prevention and adjuvant therapy of COVID-19. *The FASEB Journal*. 2020; 34: 13185 – 13193. <https://doi.org/10.1096/fj.202001807>
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Vitamin E:

Micronutrient interventions have shown a promising effect in targeting the immune system impairments observed in the elderly and improve the infection-related morbidity and mortality.

1. Maji M, Clements SJ, Ivory K, Nicoletti C, Carding SR. Nutrition, diet and immunosenescence. *Mech Ageing Dev* 2014;136_37:116–28.

Vitamin E supports the integrity of epithelial membranes and increases IL-2 production, NK cell activity, T cell-mediated functions and lymphocyte proliferation, enhances the antibody response, and activates the immune cells.

Vitamin E and selenium exhibit strong control over viral replication and mutation. In a nutritional deficiency condition of these micronutrients, RNA viruses are able to convert to more virulent strains.

Role of micronutrients:

1. Keflie TS, Biesalski HK. Micronutrients and bioactive substances: Their potential roles in combating COVID-19. *Nutrition*. 2021;84:111103. doi:10.1016/j.nut.2020.111103

2. Chowdhury, A. I. (2020). Role and Effects of Micronutrients Supplementation in Immune System and SARS-Cov-2(COVID-19). *Asian Journal of Immunology*, 4(2), 47-55.

3. Katona P, Katona-Apte J. The interaction between nutrition and infection. *Clin Infect Dis* 2008;46:1582–8. - Micronutrient deficiencies are common cause for low immunity

4. Osuna-Padilla IA, et al. Zinc and selenium indicators and their relation to immunologic and metabolic parameters in male patients with human immunodeficiency virus. *Nutrition* 2020;70:110585. - vital role of micronutrients in the prevention and treatment of viral infections

5. Hamer DH, et al. Micronutrient deficiencies are associated with impaired immune response and higher burden of respiratory infections in elderly Ecuadorians. *J Nutr* 2009;139:113–9.

Zinc: Zinc improves immune response by regulating nucleic acid synthesis and repair, apoptosis, inflammation, and redox homeostasis.

Zinc deficiency enhances the production of proinflammatory cytokines, such as IL-1b, IL-6, and TNF-a, and reduces activity of natural killer (NK) cells and retards production of antibodies.

Raised intracellular zinc level can efficiently impair CoV replication.

Selenium: Selenium deficiency & low antioxidants encourages pathogenic mutation of the virus.

Selenium deficiency impairs functions of neutrophils, T cells, lymphocytes, NK cells & thymocytes.

Iodine: Iodine secreted in the surface liquid of the upper airway has antiviral effect. Direct exposure to iodine can destroy the virus.

Copper: Used for destroying organisms after phagocytosis, it disintegrates the viral envelope & destroys the virus, also has anti viral effect by binding electron donor groups on viral proteins or nucleic acids



C-SHIELD

Iron: Iron deficiency anaemia attenuates immune response and increases susceptibility to viral infection. Iron reduces NF-kB nuclear translocation, promotes M2 & decreases proinflammatory M1 macrophage activity. Iron regulates cytokines via hepcidin. Iron oxides disintegrate the virus lipid envelope by peroxidation.

Vitamin A: Antioxidant, main regulator of mucosal immunity, inhibits viral replication, promotes immune response, decreases morbidity & mortality

Vitamin B-complex: Vitamins B1, B2, and B5 control the host immune response through the regulation of energy generation in various immune cells. Down regulate proinflammatory cytokines & NF-kB activity. Vitamin B5 activates the phagocytic activity of macrophages.

Vitamin C: Vitamin C inhibits the proinflammatory cytokines, like TNF and IL-6, promotes production of interferon, promotes the production, function, and migration of immune cells, and enhances serum values of antibodies and complement proteins. Vitamin C in high doses is viricidal.

Though these natural elements are useful they are not required in very high doses but are required to be used synergistically in a proportion that compliments the actions and enhances efficiency despite safe low dosage. The nutrients also need to be combined with supportive micronutrients to ensure complete biological utilization.

Avoid excess nutrients:

Vitamins & minerals	Adverse effects associated with supplements
Vitamin A	Hepatotoxic effects, visual change, hair and skin change, risk of lung cancer among smokers, diarrhea
Vitamin B6	Sensory neuropathy, ataxia
Vitamin B12	Diarrhea, itching, skin rash, headache, dizziness, nausea, vomiting, pulmonary edema and congestive heart failure early in treatment.
Vitamin D	Hypocalcaemia, soft tissue calcification
Vitamin C	Diarrhea, Nausea, heartburn, abdominal cramps, headache, insomnia
Vitamin E	Nausea, vomiting, diarrhea, headache, fatigue, blurred vision
Zinc	Nausea and vomiting, immune-suppression and impaired copper uptake
Selenium	Brittle hair and nails, peripheral neuropathies and gastrointestinal upset
Iron	Nausea, vomiting, reduced zinc uptake and constipation

We present a preventive therapy having each of these proven components, utilized synergistically along with micronutrients spread in a once in 3 days rotation cycle which delivers actives to work at multiple levels protecting and countering various mechanisms by which the Covid 19 virus tries to enter, replicate and spread itself. The program is aimed at protection, prevention and cure of Covid 19.

HOW TO MAKE COVID VACCINES MORE EFFECTIVE

For generating antibodies & immune response to a vaccine, the cells require amino acids, antioxidants, catalysts, coenzymes, which are all nutrients. Any deficiency compromises the immune response.

How to make COVID vaccines more effective: give people vitamin and mineral supplements

Margaret Rayman, University of Surrey, Philip C Calder, University of Southampton

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