Immune Boosting
Nutraceuticals
Immune Boosting Nutraceuticals*

It has been postulated and highly scientifically substantiated that decreased immunity is at least partially responsible for the observed increase in morbidity and mortality resulting from infectious agents, particularly in elderly. Indeed, nutritional status may explain differences in both the incidence and the pathology of infection.

Nutraceuticals encompasses a broad spectrum of available products, including dietary supplements (vitamins, minerals, herbs or other botanicals, amino acids, and substances such as enzymes, organ tissues, glandulars, pre & probiotics and metabolites) or functional foods that are intended to provide medical or health benefits, including the prevention of disease. Several nutraceuticals compounds have shown in clinical trials to exert some positive effects on immune system.

The table below shows some nutraceuticals studied that demonstrated the potential to increase the immune response, including against viruses. It is also mentioned some information about their mechanisms in immune system and dosage.

* An immunomodulator may be defined as a substance, biological or synthetic, which can stimulate, suppress or modulate any of the components of immune system including both innate and adaptive arms of immune response*. 

Agarwal & Singh, 1999
## Immune Boosting Nutraceuticals

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<th>Product/DCI</th>
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<tr>
<td><strong>Probiotics</strong>&lt;br&gt;Probiotics are live microorganisms promoted with claims that they provide health benefits when consumed (e.g. Lactobacilli, Bifidobacteria, Saccharomyces)</td>
<td>• Immunomodulation.&lt;br&gt;• Protection from viral infection&lt;br&gt;• Regulation of host innate and adaptive immune responses by modulating the functions of dendritic cells, macrophages, and T and B lymphocytes.&lt;br&gt;• Interaction with Toll receptors and modulating the levels of interleukins, TNF-α and transforming growth factor-beta (TGF-beta).</td>
<td>Probiotic pool with a dose of 100 million to 1 billion CFU per strain/day&lt;br&gt;• Personalized dose adjustments</td>
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<td><strong>Enterococcus faecium</strong></td>
<td>• Increasing the level of antibodies and macrophages activity.&lt;br&gt;• E. faecium have showed antiviral activity against gastroenteritis coronavirus.</td>
<td>200 to 600 million CFU/day</td>
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<td><strong>Licorice</strong>&lt;br&gt;(Glycyrrhiza glabra root)&lt;br&gt;dry standardized extract (20%)</td>
<td>• Immunomodulation.&lt;br&gt;• Antiviral*, antibacterial, anti-inflammatory, antioxidant and antitussive and expectorant activities.&lt;br&gt;*Glycyrrhizin (phytochemical presents in Licorice) have reported as an effective inhibitor of viral adsorption and penetration into the cells. Glycyrrhizin has the potential binding to ACE2 inhibiting the viral replication. Angiotensin-convertin enzyme 2 is used by SARS-CoV-2 to enter in cell receptor).&lt;br&gt;The low toxicity of glycyrrhizin, and anti-virus effects on SARS and its potential interaction with ACE2, it’s worthwhile way to fight against COVID-19.</td>
<td>250 to 500mg 3x/day</td>
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<td><strong>Astragalus</strong>&lt;br&gt;(Astragalus membranaceus)&lt;br&gt;dry standardized extract (70%)</td>
<td>• Immunomodulation&lt;br&gt;• Macrophage activation&lt;br&gt;• Enhacing immunoglobulin production to restoration of lost T-cell activity&lt;br&gt;• Antiviral activity</td>
<td>100mg twice a day</td>
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| **Cordyceps** (C. sinensis)   | • Immunomodulation  
• Antioxidant & anti-inflammatory  
• Macrophage activation to produce proinflammatory cytokines  
• Regulating innate and adaptive immunity. | 525 - 625mg 1-2x/day at meals. |
| **Equinacea** (E. purpurea)   | • Immunomodulation  
• Anti-inflammatory effect  
• TNF-α and IL-6 control  
• Regulation of immune system  
• Prevention of upper respiratory infections. | 200mg 3x/day                |
| **Ganoderma** (G. lucidum)    | • Immunostimulant effect  
• Increase the activity of NK cells, T-cells.  
• Increase CD4 cells  
• Phagocytosis stimulation  
• Antiviral (RNA viruses) replication inhibition activity  
• Platelet aggregation inhibition | 200mg 3x/day                |
| **Royal jelly**               | • Immunomodulation  
• Antioxidante | 300mg 2x/day                |
| **L-lysine**                  | • Immunocompetence (e.g. antibody formation)  
• Can help in herpes infections | 500 to 1500mg/day            |
| **Maitake** (G. frondosus)    | • Immunomodulation  
• Increase response of NK-cells and macrophages, cytotoxicity activity of T-cells, and antigen-antibody response  
• Increase INF-γ and IL-2 production by macrophages. | 300mg 3x/day                |
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<td><strong>Propolis</strong>&lt;br&gt;Product derived from resinous substances, gums and balsamic, harvested by bees, from shoots, flowers and exsudates of plants. Anti-inflamatória, bactericida, fungicida. <em>The propolis activities can vary between different types of propolis (brown, green or red types)</em></td>
<td>• Immunomodulatory&lt;br&gt;• Increasing macrophages microbiocidal activity&lt;br&gt;• Stimulation action of NK cells against tumor cells, and on antibody production&lt;br&gt;• Anti-inflammatory&lt;br&gt;• Activity anti-viral, anti-bacterial, and antifungal.</td>
<td>Dry extract&lt;br&gt;200 - 1000mg/day&lt;br&gt;Tincture&lt;br&gt;10 drops 3x/day</td>
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<td><strong>Rose hips</strong>&lt;br&gt;(Rosa canina)&lt;br&gt;dry standardized extract (30% of vitamin C)</td>
<td>• Antioxidant&lt;br&gt;• Similar benefits of vitamin C</td>
<td>Dosage in terms of vitamin C content&lt;br&gt;Adults: 50 - 100mg/day&lt;br&gt;Children (4 - 6 years old): 45mg/day</td>
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<td><strong>Complex B vitamins</strong>&lt;br&gt;Vitamin B₁&lt;br&gt;Vitamin B₆&lt;br&gt;Vitamin B₁₂</td>
<td>• Improvement of vitamin deficiencies&lt;br&gt;• Modulation of immune system&lt;br&gt;• Improvement of neuropathic symptoms</td>
<td>B₁₂: 250 - 750mcg/day&lt;br&gt;B₆, B₉: 750mg/day&lt;br&gt;B₁₂: 30 - 75mcg/day</td>
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<td><strong>Vitamin C</strong></td>
<td>• Antioxidant (protection cell against the oxidants releases by phagocytes).&lt;br&gt;• Enhances T-cell function and proliferation.&lt;br&gt;• Enhances the proliferation of NK cells&lt;br&gt;• Improvement of common cold, flu and functionality of immune system, reduction of severity of infections and its symptoms.&lt;br&gt;• Prevents the susceptibility to lower respiratory disease.&lt;br&gt;• Patients vitamin C supplemented can have lower incidence of pneumonia caused by SARS coronavirus.</td>
<td>Adults: 250 - 1000mg/day&lt;br&gt;Children: 40 - 60mg/day</td>
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| **Vitamin D3**  
(cholecalciferol) | • Modulation of response innate and adaptative  
• Antiviral and antibacterial effect  
• Modulation of B cell proliferation and differentiation.  
• Increase immunoglobulin secretion.  
• Increase lymphocytes T e B proliferation and maturation  
• Decrease of the viral replication  
• Increasing defense against respiratory infections  
• Decreasing symptoms of rhinovirus infection  
• Vitamin D status had been reported to cause the infection of bovine coronavirus | 2,000 - 5,000IU/day |
| **Zinc** | • Zinc supports the effective function and proliferation of various immune cells.  
• Zinc is crucial for normal development and function of cells mediating nonspecific immunity as neutrophils and NK cells.  
• Improvement of humoral immune response.  
• Age-Related Eye Disease multicenter study has observed significant reduction of mortality in elderly population treated of high dose zinc.  
• Low concentration of intracellular zinc inhibits the replication of SARS coronavirus (SARS-CoV)  
• Zinc supplement may have effect not only on COVID-19 related symptom like diarrhea and lower respiratory tract infection. | Adults: 25 - 50mg of elementar zinc/day |
| **Selenium**  
(as selenomethionine) | • Takes part in the beginning of immune response.  
• Important for innate and adaptative immune response.  
• Stimulation of T helper lymphocytes, cytotoxic T and NK cells, macrophage phagocytosis.  
• Synergistic effect with ginseng could be induce immune response against viruses.  
• Antioxidant.  
• Dietary selenium deficiency causes oxidative stress and can alter a viral genome so that a normally benign or mildly pathogenic virus can become more virulent under oxidative stress condition.  
• Deficiency in selenium induces impairment of host immune system and mutation of benign variants of RNA viruses to virulence.  
• Potential to help prevent and control RNA virus infections (including COVID-19 virus) by amplifying the signalling functions of toll-like receptor 7 (TLR7).  
• Selenium supplementation could bring benefits RNA viroses (COVID-19). | 50 - 100mcg/day  
Duration of treatment: cyclic  
(usually 30 - 120 days) |
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| **N-acetylcysteine**        | • Help prevent and control RNA virus infections by amplifying functions of TLR7 and mitochondrial antiviral-signaling protein (MAVS) in evoking type 1 interferon production.  
                               • Supplementation of 600mg twice a day has reduced significantly fewer influenza-like episodes and days of bed confinement.                               | 1200 - 1800mg/day |
| **Alpha-lipoic-acid (ALA)** | • Boosting type 1 interferon response.                                                                                                                                                                                 | 600 - 1800mg/day  |
| **Ferulic acid**            | • Activation of TLR7  
                               • Induction of heme oxygenase-1 (HO-1).  
                               • Stimulation type 1 interferon production.  
                               • Help prevent and control RNA virus infections by amplifying the signalling functions of TLR7 and MAVS.                                                                 | 3000 mg or more/day |
| **Glucosamine**             | • May up-regulating MAVS activation.  
                               • Might aid prevention and control of RNA virus infections.                                                                                                                                                  |                 |
| **Spirulina**               | • Increasing rate of production of RBCs and WBCs by enhancing hematopoiesis.  
                               • Direct effect on both innate and specific immunity.  
                               • Activation of macrophage and NK cells and T-cells.  
                               • Inducing production of antibodies.  
                               • Phycocyanobilin present in Spirulina and in other blue-green algae may have potential for boosting type 1 interferon response in the content of RNA virus infection.  
                               • Phycocyanin has been found to decrease mortality in influenza-infected mice.                                                                                                                               | 3 - 15g/day     |
| **Elderberry**              | • Symptomatically beneficial in influenza and the common cold.  
                               • Probably its impact on viruses might be mediated by anthocyanin metabolite (ferulic acid).  
                               • Inhibition the replication of influenza virus type A and B (in vitro).  
                               • Decreasing of human influenza virus (H1N1) (in vitro)  
                               • Decreasing the duration of illness in patients with influenza.                                                                                                                                              | 600 - 1000mg     |
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<td><strong>Trans-resveratrol</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td>• Atioxidant&lt;br&gt;• Resveratrol regulates immunity by interfering with immune cell regulation, proinflammatory cytokines synthesis, and gene expression.&lt;br&gt;• Increasing plasma level of interferon gamma and natural killer (NK) cells.&lt;br&gt;• At the molecular level, it targets sirtuin, adenosine monophosphate kinase, nuclear factor- <strong>B</strong>, inflammatory cytokines, antioxidant enzymes along with cellular processes such as gluconeogenesis, lipid metabolism, mitochondrial biogenesis, angiogenesis, and apoptosis.&lt;br&gt;• Resveratrol can suppress the toll-like receptor (TLR) and pro-inflammatory genes' expression.</td>
<td>&gt;150mg/day&lt;br&gt;Cyclic use</td>
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<td><strong>Ginseng</strong>&lt;sup&gt;2&lt;/sup&gt;</td>
<td>• Reduction in the incidence of common cold, flu, and enhancement of the immune response.</td>
<td>100 - 300mg 2x/day</td>
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<td><strong>Magnesium</strong></td>
<td>• Immune disorders associated with magnesium deficiencies.&lt;br&gt;• Immune system regulation&lt;br&gt;• Cofactor in more than 300 enzymatic reactions involving energy metabolism and nucleic acid synthesis.</td>
<td>400 - 600mg&lt;br&gt;(cyclic 30 - 90 days)</td>
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<td><strong>Rhodiola</strong>&lt;sup&gt;3&lt;/sup&gt;</td>
<td>• Improvement of immunity mediated by T cells and macrophage response.</td>
<td>340 - 680mg/day&lt;br&gt;Cyclic (usually 30 - 90 days)</td>
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<td><strong>Green tea</strong></td>
<td>• Inhibition the growth of influenza virus by (-) epigallocatechin (virus) phytochemical present in Green tea.&lt;br&gt;• Reducing the number of days with cold or flu symptoms.</td>
<td>250 - 500mg/day&lt;br&gt;(Cyclic)</td>
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<sup>1</sup> Polyphenolic stilbenoid, present in grapes, mulberries, peanut, rhubarb and several other plant, that plays an important role in a large variety of biological activities.

<sup>2</sup> (Panax ginseng)<br>4-5% ginsenosides

<sup>3</sup> (Rhodiola rosea)<br>dry standardized extract
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| Vitamin A (retinol)                                                        | • Protection of the skin and mucous membranes (first line defense barrier against bacteria, viruses and parasites.  
• Reducing morbidity and mortality in different infectious diseases  
• Antibody production  
• Activation of macrophages, NK cells and lymphocytes | 2666 - 5000IU  
Additional protection against infections: 10,000IU (cyclic) |
| Betacarotene and carotenoids                                               | (lycopene, astaxanthin, zeaxanthin, lutein)  
• Immune modulator: increased NK cell activity, proliferation of B and T cells. | Betacarotene: 10,000 - 30,000 IU mg/day  
Lycopene: 5 - 10mg/day  
Astaxanthin: 1 - 12mg  
Lutein: 2 - 6mg/day  
Zeaxanthin: 2mg/day |
| Omega-3 (EPA-DHA)                                                          | • Omega-3 including protectin D1 (omega-3 PUFA/derived lipid mediator), which served as a novel antiviral drug. | 2 - 6g/day                                  |
| Collostrum                                                                 | • Stimulation of B lymphocytes  
• Increases the activity of macrophages.  
• Contains immunoglobulins and lactoferrin that play roles in immune system. | 500 - 1000mg 1 - 3x/day                     |
| Agaricus blazei dry standardized extract                                   | (10% polysaccharides)  
Mushroom rich in immunomodulator fibers: α-glucans, proteoglycans, heteroglucans, chitin e peptideoglycans. | 400mg 3x/day                                 |
|                                                                           | • Immunomodulation effect.  
• Stimulation of clonal expansion of T-cells, NK cells, macrophages, monocytes, B lymphocytes  
• Increase antibodies and cytokines production, complements. |                                            |
References

3. MC CARTY M.F., DiNICOLANTONIO J.J. Nutraceuticals have potential for boosting the type 1 interferon response to RNA viruses including influenza and coronavirus, https://doi.org/10.1007/978-1-4020-3658-5_16