

## Immune Health: Nutritional Bioactives

Bioactive	Mechanisms
Andrographis ( <i>Andrographis paniculate</i> ) <sup>1,2</sup>	Used in Ayurvedic medicine as a powerful tonic for the respiratory tract and supporting a healthy immune response.
Berberine <sup>4</sup>	Shown to have significant antimicrobial activity against bacteria, fungi, and viruses.
Epigallocatechin gallate (EGCG) <sup>8-10</sup>	EGCG, a polyphenol commonly found in green tea, suppresses NLRP3 inflammasome mRNA activation and oxidative stress. EGCG inhibits NF-κB activation and reduces expression of multiple inflammatory signals such as TNFα, IL-6, iNOS, and MMPs. It also has antioxidant properties.
Medicinal mushrooms including: reishi ( <i>Ganoderma lucidum</i> ), shiitake ( <i>Lentinus edodes</i> ), cordyceps ( <i>Paecilomyces hepiali</i> Chen) <sup>11,12</sup>	May support the body's defense system against infections by acting on various elements of the immune system and increasing a Th1 type of immune response.
Melatonin <sup>13</sup>	Effective inhibitor of NLRP3 activation via a variety of mechanisms.
N-acetyl cysteine (NAC) <sup>14-16</sup>	NAC is a precursor in the production of glutathione, and supplementation can increase tissue glutathione levels in humans. In an experimental model of reactive oxygen species (ROS)-triggered NLRP3 expression, treatment with NAC suppressed the activation of the inflammasome. NAC regulates mRNA expression of lipopolysaccharide (LPS)-triggered NLRP3 inflammasome, lowering cytokines such as IL-1β.
Omega-3 fatty acids (EPA and DHA) <sup>17-19</sup>	May exert beneficial effects on the immune system at multiple levels including regulation of gene expression, signal transduction pathways, and the production of eicosanoids and cytokines.
Perilla seed extract ( <i>Perilla frutescens</i> ) <sup>21</sup>	Perilla inhibits the production of cytokines (ie.IL-4, IL-10), TNF-α, and histamine release and reduces IgE levels.
Probiotics ( <i>Saccharomyces boulardii</i> , <i>Lactobacillus paracasei</i> 8700:2, <i>Lactobacillus plantarum</i> HEAL9) <sup>22-24</sup>	Immune-modulating functions that are well-established include contributing to a diverse microbiome and improving gastrointestinal barrier function.
Quercetin <sup>25-29</sup>	Quercetin, a polyphenol found in many fruits and vegetables, has been shown to reduce the expression of NLRP3 inflammasome components and secretion of proinflammatory cytokines such as IL-1β. Quercetin helps ameliorate mitochondrial dysfunction and endoplasmic reticulum stress, suppressing ROS formation in inflamed tissues.
Selenium <sup>30,31</sup>	Deficiency has been associated with more severe viral disease. Selenium is required for defense mechanisms associated with neutrophils, macrophages, natural killer cells, and T lymphocytes to function appropriately. Antioxidant properties associated with selenium can sequester ROS produced by the invading pathogen.

Bioactive	Mechanisms
Specialized pro-resolving mediators (SPMs) <sup>32-37</sup>	SPMs, bioactives that can be found in specialized fractions of fish oil, promote inflammation resolution without causing immunosuppression and enhance pathogen phagocytosis in immune cells. SPM RvD2 blocks NLRP3 inflammasome activation, reduces IL-1 $\beta$ , and reprograms macrophages to a proresolving phenotype.
Thyme ( <i>Thymus vulgaris</i> ) <sup>38</sup>	Traditionally used to support the health of the lungs and bronchials. Source of thymol and carvacrol, compounds that have complementary activity in supporting intestinal microbial balance.
Vitamin A <sup>39</sup>	Plays a role in mucosal membrane integrity. Vitamin A regulates mechanisms responsible for the control and resistance against both bacterial and viral infections (i.e./glycoprotein structure, antigen presenting cells, T-cell maturation, etc.).
Vitamin C <sup>40-42</sup>	May reduce the risk, severity, and duration of infectious diseases. Vitamin C has been found to stimulate leukocyte function, especially neutrophil and monocyte movement. Preclinical evidence suggests vitamin C inhibits NLRP3 activation through scavenging mitochondrial reactive oxygen species (ROS), rather than by inhibiting NF- $\kappa$ B.
Vitamin D <sup>43-48</sup>	Ability to modulate both innate and adaptive immune systems via defensin proteins activation and cell-membrane disruption. Regulates inflammasome activation through vitamin D receptor (VDR) binding directly bind to NLRP3 and prevents the inflammasome from assembling.
Zinc <sup>49-51</sup>	Zinc is a vital nutrient for proper immune function. Zinc deficiency (especially common in older populations) in immune cells activates the NLRP3 inflammasome, induces IL-1 $\beta$ secretion, and contributes to inflammation. Zinc inhibits NLRP3 by activating the Nrf2 antioxidant pathway and reduces the production of ROS.

#### Acronyms:

**NLRP3:** NOD-, LRR-, and pyrin domain-containing protein 3

**mRNA:** messenger ribonucleic acid

**NF- $\kappa$ B:** nuclear factor kappa-light-chain-enhancer of activated B cells

**TNF $\alpha$ :** tumor necrosis factor alpha

**IL:** interleukin

**iNOS:** nitric oxide synthase

**MMPs:** matrix metalloproteinases

**RvD2:** resolvin D2

**Nrf2:** nuclear factor erythroid 2-related factor 2

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