

# Antiviral Functional Foods

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Functional foods optimize the immune system capacity to prevent and control pathogenic viral infections. Functional foods prevention of non-communicable disease can be translated into protecting against respiratory viral infections and COVID-19. Foods with antiviral properties include fruits, vegetables, fermented foods and probiotics, olive oil, fish, nuts and seeds, herbs, roots, fungi, amino acids, peptides, and cyclotides.

Keywords: Functional food, coronavirus, immunity, lifestyle

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## 1. Introduction

Viral infections are responsible for significant global morbidity and mortality rates across the world, and viral outbreaks such as novel coronavirus (COVID-19) <sup>[1]</sup>. Reports from the World Health Organization (WHO) estimate 3–5 million hospitalized cases of seasonal influenza severe illness, resulting in 290,000–650,000 annual deaths <sup>[2]</sup>. Currently, COVID-19 is causing a health crisis across the world. Limiting the spread of infections in the short and medium terms involves a number of preventative public health practices including regular hand washing, covering coughs, lockdown, and social distancing measures. Vaccines have been implemented for preventing and controlling several viruses over the past century and have also been used for preventing common influenza <sup>[3][4]</sup>. However, influenza vaccine development takes a significant amount of time <sup>[5]</sup>, which necessitates alternative complementary remedies for COVID-19. Furthermore, antiviral medication treatments face continuous challenges in terms of drug dose and selection and intervention phase, especially during acute respiratory infections <sup>[6]</sup>.

Lifestyle approaches could play an essential antiviral long-term preventative role. The antiviral role of nutrition and exercise as the two lifestyle prevention pillars has received little research attention. In particular, how the antiviral immunological defence capacity could be enhanced using functional foods, nutraceuticals, and physical activity behaviors, whether such behaviors are alone or combined. Functional foods and nutraceuticals can be safe and cost-effective strategies to enhance the immune system and provide protection from pathogenic viral infections. For example, optimal intake of selected micronutrients has been highlighted in controlling the impact of virulent strain infections, including lower and upper respiratory tract infections, through optimizing a well-functioning immune system <sup>[7]</sup>.

## 2. Importance of Functional Foods in Preventing Communicable Disease and COVID-19

Functional foods naturally possess active ingredients or “nutraceuticals” that are associated with disease preventative health benefits are now widely accepted for the prevention and management of major NCDs, especially those characterized by inflammatory and oxidative stress disorders such as diabetes and cardiovascular disease <sup>[8][9]</sup>. However, less is known about the role of functional foods in communicable diseases (CDs), especially on the immune system defence against viral infections such as COVID-19. A variety of fruits, vegetables, oily fish, olive oil, nuts, legumes are all considered functional foods based on their natural contents of nutraceuticals, including polyphenols, terpenoids, flavonoids, alkaloids, sterols, pigments, and unsaturated fatty acids <sup>[8][10]</sup>. Polyphenol-rich herbs, especially coffee, differently fermented teas (green, black) and yerba maté, have also shown to have various effectiveness on metabolic and microvascular activities, cholesterol and fasting glucose lowering, anti-inflammation and anti-oxidation in high-risk populations <sup>[8][11]</sup>. Bioactive peptides, naturally present in food proteins or formulated as nutraceuticals based on their molecular weight, amino acid chain length, or peptide composition, have also been postulated to elicit versatile physiological responses associated with immunological, antimicrobial, cardiovascular, gastrointestinal, neurological, and other hormonal activities of the human system <sup>[12]</sup>. Such functional food benefits can be translated to protect against viral infections and COVID-19.

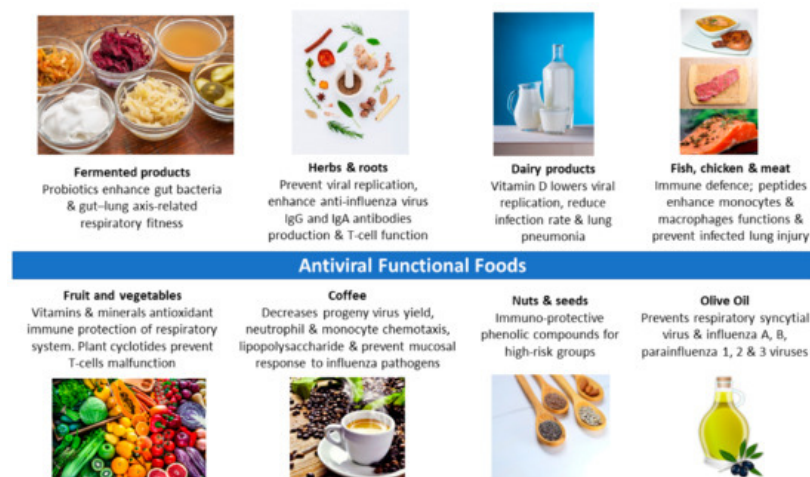
Viral infections are characterized by a compromised immune function and deficient micronutrient stores, particularly vitamins, including vitamins A, B6, B12, C, D, E, and folate, and trace elements, including zinc, iron, selenium, magnesium, and copper [7]. Evidence already supports an efficient function of the immune system through consuming those various nutraceuticals within a variety of functional foods including essential fatty acids, linoleic acids, essential amino acids, and the aforementioned vitamins and minerals, especially where forms of immunity may be affected by deficiencies in one or more of these nutraceuticals [13][14]. Adequate dietary intake, and supplementation of such functional foods, contribute to maintaining optimal levels in the human body, which enhances several aspects of the immune system [7][15], and provides an important antiviral prevention of COVID-19 [16]. Conversely, less robust immune responses have been shown to be the primary risk factor for COVID-19 [17], which makes it timely to describe the protective role of functional food component benefits in the context of preventing COVID-19 and seasonal infections.

In terms of jointly addressing NCD and CD prevention within high-risk populations, investigating the functional foods effects on CDs including COVID-19 is particularly important. Higher infection and mortality rates related to COVID-19 have been documented among older adults and patients with obesity, cardiac diseases, hypertension, or diabetes [18]. For example, COVID-19 statistics in England showed that almost a third (31.3%) of COVID-19-related mortalities had type-2 diabetes [19], while there was a two-fold increase (86%) in requiring mechanical ventilation among COVID-19 infected obese individuals compared with (47%) of infected healthy weight individuals [20]. The prevalence of NCDs, especially diabetes amongst high-risk groups, is becoming a matter of emerging importance, and diabetes is now considered a risk factor for the progression and prognosis of COVID-19 [21][22]. Therefore, optimal “immune-enhancing” functional foods combined with behavioral lifestyle approaches (especially exercise) could provide an optimal prevention of the double burdens of NCD and CD multimorbidity.

Various dietary patterns contain functional food components that have been promoted in the past for NCD prevention, especially the vegetarian diet, the Nordic diet, or the Mediterranean diet (MD), and its combination with other lifestyle approaches [8][9][23][24]. Common functional foods within those diets include plant-based fruit and vegetables such as olive oil and tree nuts, seeds, fish, dairy products, and herbs, teas, and fermented products, which contain key nutraceuticals with disease protective anti-inflammatory and anti-oxidation properties [8][24][25]. Established health protective functional components include monounsaturated fatty acids (MUFA) such as oleic acid in olive oil, omega-3 polyunsaturated fatty acids (e.g., alpha-linolenic acid) found in tree nuts such as walnuts, eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) found in oily fish, high amounts of polyphenol flavonoids and antioxidants found in fruit and vegetables, and high amounts of fiber found mainly in cereal and whole-grain foods [24]. Consuming those functional foods, and their components vary across geographical global regions [8][11][24][26][27][28], but what is agreed on is their cardiometabolic protective benefits of reducing major NCDs and mortality risks [8][23][29]. The challenge is to translate such functional effects towards enhancing and protecting the immune system and its antiviral defence response into the prevention of emerging CDs such as COVID-19.

### **3. Conclusions and Recommendations**

Functional foods may provide a further effective diverse antiviral approach and could have a joint prevention of both NCDs and CDs among diverse populations. Dietary intake of foods rich in vitamins and minerals can be increased to provide an immune boost, especially in individuals with deficiency in these micronutrients. Increased intake of probiotics, omega-3 from fish, protein peptides from chicken and fish, and olive-based products are also recommended (Table 1, Figure 1). There is no specific model to follow to enhance the immune system against COVID-19. However, the more varied the dietary sources, the better the protection is against all viral infections. Adopting exercise together with an enhanced dietary intake of functional compounds may contribute as a preventative medicine against emerging viral infections.



**Figure 1.** Functional foods and antiviral mechanisms to optimize health.

**Table 1.** Antiviral functional foods, their immune protective nutraceuticals, mechanisms of action, and recommended intake.

Antiviral Functional Foods	Immune-Promoting Nutraceuticals	Key Mechanisms of Action	Antiviral Targeted Recommendations
Fruit & vegetables	Vitamins: C, B2, B6, and B12, folic acid, beta carotene, iron, plant cyclotides	Promote antioxidation and anti-inflammation properties, protect the respiratory system, and reduce risks of infection and re-infection [14]. Cyclotides protect against infections and pathogens by preventing malfunctioning of the immune cells (T-cell lymphocytes), which reduces over-reactivity of this defence machinery during infections [30].	Intake is highly recommended as part of a balanced diet. Complements an active lifestyle, supports circadian rhythm, and sleep quality
Dairy products	Vitamins D, A, & E	Vitamin D reduces the risk of contracting respiratory infections and COVID-19 [16][31]. Lowers viral replication rates through cathelicidins and defensins, and prevents lung injuries that lead to pneumonia through anti-inflammatory cytokines [32].	Dietary intake is preferred. Supplements (zinc, selenium, and vitamin D) are recommended in older adults and the most deficient. Enhances sleep quality.
Seeds and nuts	Zinc, selenium, copper, trace minerals	Contain phenolic compounds that are immunoprotective particularly through antioxidative and anti-inflammatory properties in high-risk adults [8].	Supplementation is recommended when dietary intake is low, especially in older and high-risk individuals
Fish & seafood	EPA & DHA Omega-3	Support inflammatory resolution and healing of infected sites including the respiratory tract, which could prevent acute lung injury, mainly through pro-resolving mediators (SPMs) such as resolvins, protectins, and maresins [7].	Increased intake is recommended in high-risk individuals
Protein rich foods (e.g., red meat, chicken, seafood)	Amino acids and peptides: Anserine, carnosine, taurine, creatine, and 4-hydroxyproline, vitamins, iron, copper	Dietary intake of anserine and carnosine promote immunological defence against infections by bacteria, fungi, parasites, and viruses (and coronavirus) through enhanced immune cell functions of monocytes and macrophages [33][34]. Plant peptides (e.g., soybean) increase lymphocytes and granulocytes; enhance natural killer activity [35].	Dietary intake is sufficient, but an increased intake is recommended in high-risk individuals and infected patients. Can be obtained from both animal and plant sources.
Olive based products (olive oil, olive leaves)	Oleuropein, hydroxytyrosol, elenolic acid, vitamin E	Reduced upper respiratory infection attributed to antioxidative property of oleoic acid in oleuropein, especially influenza A and B, parainfluenza 1, 2, and 3 viruses, and herpes [36].	Dietary intake (20–30 g/day), especially from extra-virgin olive oil, which is high in polyphenol content. Increase benefits with physical activity.

Antiviral Functional Foods	Immune-Promoting Nutraceuticals	Key Mechanisms of Action	Antiviral Targeted Recommendations
Coffee (coffee leaves, differently fermented)	Caffeic acid, caffeine, polyphenols, chlorogenic acid	Caffeic acid decreases the progeny virus yield (especially within 3 h post-infection) and suppresses the degeneration of the virus-infected cells; caffeine can suppress of neutrophil and monocyte chemotaxis, and pro-inflammatory cytokines (e.g., TNF- $\alpha$ ) <sup>[37]</sup> . It suppresses endotoxins LPS-induced inflammatory responses (regulates NF- $\kappa$ B activation and MAPK phosphorylation) <sup>[38]</sup> , and prevents mucosal response to pathogens infecting the respiratory tract and influenza viruses <sup>[39]</sup> .	Coffee intake (2–3 cups/daily) is recommended and has superior immunological benefit to caffeine supplementation since it is more wholesome (contains both caffeic acid and caffeine).
Roots & fungi, traditional herbs, and medicinal plants	Maoto, licorice roots, cordyceps mushrooms, Chinese mushrooms, ginseng	Herbs and roots prevent viral replication, enhance anti-influenza virus IgG and IgA antibodies production, and improve T-cell function <sup>[40]</sup> . Glycyrrhizin (in Maoto) helps progeny influenza viruses to leave without re-infecting, inhibits influenza A virus uptake into the cell and reduces CCID50 by 90% <sup>[41]</sup> . Ginseng and cordyceps have antioxidative (GSH, SOD) and cell senescence angiogenesis properties <sup>[42]</sup> .	Dietary intake is highly recommended. Supplement when dietary intake is low (e.g., cordyceps, 1.5 g/day).
Fermented foods & probiotics	Yoghurt, kaffir, pickles, fermented fruits, vegetables and plants, probiotic drinks	Microbiota especially lactobacilli and bifidobacterial enhance gut bacteria profile and gut–lung axis-related respiratory fitness <sup>[43][44]</sup> .	Dietary intake of fermented foods is recommended

COVID-19, Novel corona virus-19; EPA, Eicosapentaenoic acid; DHA, Docosahexaenoic acid; GSH, Glutathione; SOD, Superoxide dismutase; IgG, Immunoglobulin g; IgA Immunoglobulin A; LPS, Lipopolysaccharides; TNF- $\alpha$ , Tumor necrosis factor-alpha; NF- $\kappa$ B, Nuclear factor- $\kappa$ B; MAPK, Mitogen-activated protein kinase.

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