

Vitamins, Minerals and Other Elements of the Diet for Strengthening the Immune System and Reduce the Burden of Viral Respiratory Tract Infections: A Review

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Abstract

Viral infections of the respiratory system comprise a broad spectrum of mild to life-threatening diseases that inflict a significant clinical, humanitarian and economic burden to societies. The intake of an adequate caloric-protein diet rich in micronutrients is a modifiable factor to decrease the load of viral respiratory tract infections in the population. Micronutrients are essential to strengthen the immune system. The objective of this review is to summarise the most consistent evidence that substantiates a potential role of vitamins, oligoelements, probiotics and herbs to reduce the clinical burden of viral respiratory tract infections. Electronic sources of medical publications (PubMed and Scopus) were searched to identify literature reviews, meta-analyses and clinical studies on the health outcomes of using dietary elements in the context of viral infections of the respiratory system. Overall, vitamins C and D as well as zinc, selenium and probiotics are at the cornerstone for strengthening the immune response to viral respiratory infections. Vitamin C and D are fundamental for ameliorating the burden of acute infections of the upper respiratory tract as well as pneumonia, particularly in high risk individuals and in patients who have low vitamins plasma levels. Probiotics are essential to guarantee the diversity and good balance of the microbiota of epitheliums. Probiotics may have a significant role in the recovery of critically ill patients after viral infections of the respiratory tract. Herbs and botanical extracts help diminishing the number and length of symptoms. All these elements of the diet exert some immunomodulatory effect that improves the response to anti-viral vaccination. More research is needed to precise the role of micronutrients and other common elements of the diet to inform their most appropriate and correct use.

Keywords: *Viral Infections; Respiratory System; Immunity; Diet; Micronutrients; Probiotics; Review*

Abbreviations

CI: Confidence Interval; HR: Hazard Ratio; OR: Odds Ratio; RCT: Randomized Clinical Trial; ROS: Reactive Oxygen Species; RR: Relative Risk; SARS: Severe Acute Respiratory Syndrome; URI: Upper Respiratory Tract Infection

Background

Viral infections of the respiratory system comprise a broad spectrum of diseases, from mild forms of common colds in the upper respiratory tract to serious and life-threatening pneumonia of the lungs. Viral respiratory infections are a significant disease and economic

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burden for societies as well as a common reason for impaired health related quality of life in individuals of any age [1]. At one end of the spectrum, common cold and cough are a frequent cause of work and school absenteeism and productivity loss [2]. At the other end of the spectrum, pneumonia is one of the most common serious infections among young children in low-income countries and among the elderly in high-income populations [3].

Influenza virus, respiratory syncytial virus and parainfluenza have been constantly more frequently reported in adults while coronaviruses causing severe acute respiratory syndrome (SARS) have nowadays gained the greatest consideration [4]. In this sense, the 2002 - 2004 SARS outbreak in Asia may serve as a reference of the potential impact that SARS coronavirus epidemics may have on the health and economy of populations. The 2002 - 2004 SARS outbreak resulted in a highly contagious and potentially life-threatening form of pneumonia that killed about 1 in 10 people who were infected [5]. Although it was eventually brought into control in 2003, its economic impact has been estimated in the range of 0.5% - 1% of the annual gross domestic product across the affected economies in the Asia-Pacific Economic Cooperation region, with unequal effects across sectors [6].

The intake of an adequate caloric-protein diet rich in micronutrients is a most important modifiable factor to decrease the burden of viral respiratory tract infections in the population [7]. Many clinical studies have demonstrated the beneficial effects of adequate micronutrients intake on the immune system. Micronutrients are essential to maintain and strengthen the immune system through their action on epithelial barriers, cellular immunity and antibody production [8]. However, about 2,000 million people have been estimated to suffer from micronutrient deficiency globally [9]. Deficiencies commonly exist for zinc, iron, iodine and vitamins A, C, D and E, and are prevalent in pregnant women and children due to higher physiological demands [10] but also in the aged populations, smokers, overweight individuals, in persons living in zone of the globe with highly contaminated air, and in populations from developing countries due to inadequate or insufficient nutrition [11]. While micronutrient deficiencies may favour viral respiratory tract infections, infections may also cause nutrition deficits that further alter the nutritional status of the individual resulting in a vicious cycle [12].

Although the information on the precise role of micronutrients on reducing the burden of viral infections of the respiratory tract appears inconsistent, there seems to be sufficient clinical data showing that incorporating multiple micronutrients with immune-supporting roles may modulate immune function and reduce the risk of viral respiratory infections [13]. The objective of this review is to summarise the most consistent evidence appeared since the year 2000 onwards that substantiates the potential role of vitamins, oligoelements, probiotics as well as herbs and botanical extracts on the prevention and management of viral respiratory tract infections. Several electronic sources of medical publications (PubMed and Scopus) have been searched to identify literature reviews, meta-analyses and clinical studies on the health outcomes of using dietary elements to diminish the burden of viral infections of the respiratory system.

Vitamin C

Vitamin C, known as L-ascorbic acid, develops crucial biosynthetic and antioxidant activities, improves the absorption of iron and has an important role in the immune system in actions needed to contend viral respiratory infections (Table 1) [14].

Many studies have examined the effects of vitamin C on viral respiratory infections with diverse results. It has been found that large doses of vitamin C in excess of 1g daily taken at onset and for the following days of a common cold do not reduce the duration or severity of cold symptoms when compared with a dose of vitamin C below the minimum recommended daily intake providing no justification

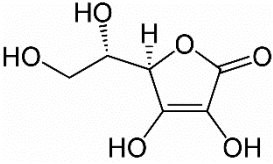
Vitamin C	Role of vitamin C in the immune system	Beneficial effects in viral respiratory infections
	<ul style="list-style-type: none"> In epithelial barriers: <ul style="list-style-type: none"> ↑ Collagen synthesis and stabilization Protect against ROS-induced damage ↑ keratinocyte differentiation ↑ fibroblast proliferation and migration 	↓ Duration
	<ul style="list-style-type: none"> In phagocytes: <ul style="list-style-type: none"> Acts as an antioxidant ↑ phagocytosis and ROS generation ↑ microbial killing Facilitates apoptosis ↓ necrosis 	↓ Severity
	<ul style="list-style-type: none"> ↑ differentiation and proliferation of B and T lymphocytes ↑ antibody levels Modulates cytokine production 	↑ Relief of symptoms
	<p style="text-align: center;">ROS: Reactive Oxygen Species</p>	Preventive effect

Table 1: Vitamin C function in the immune system and beneficial effects in viral respiratory infections [14].

for using high doses of vitamin C for common cold [15]. Likewise, a Cochrane review found that that routine mega-dose use of vitamin C in the prophylaxis of common colds is not rationally justified for community supplementation in the normal population. But it could be warranted in persons exposed to brief periods of severe physical exercise and/or cold environments.

Furthermore, a consistent reduction of cold duration of 8% (95% CI 3% to 13%) was observed in adults, and of 13.5% (95% CI 5% to 21%) in child participants. Regarding the severity of episodes, the pooled results revealed a difference favouring those participants on vitamin C. The number of days confined to home and off work or school (p = 0.02), the severity of symptom (p = 0.16) and both measures combined (p = 0.004) were reduced [16]. A more recent meta-analysis also demonstrated that therapeutic doses of vitamin C could help to reduce the duration of a common cold to about half a day, to shorten the time confined indoor by about 10 hours and to relieve symptoms of a common cold, such as chest pain, fever and chills [17].

In children, a meta-analysis (n = 3,135 children) showed that the use of vitamin C decreased the duration of upper respiratory tract infections (URTI) by 1.6 days (standardized mean differences = -0.30; 95% CI: -0.53; -0.08; p = 0.009; I² = 70%) [18]. Although no

preventive effects were found, the authors suggested that given the frequency of URTI, the inappropriate use of antibiotics, and the safe nature of vitamin C, its supplementation would be justified, especially in children under 6 years of age and those who present a high frequency of URTI [18].

Regarding the use of vitamin C for ameliorating the burden of community-acquired pneumonia, there is evidence for a lower incidence, lower mortality and reduced severity among children and young adults at or near the end of the socio-economic status, the elderly and the most ill patients, all sectors of the population in whom dietary vitamin C intake was most probably low. Therefore, vitamin C supplementation may be reasonable for pneumonia patients who have low vitamin C plasma levels [19].

Vitamin D

Vitamin D is a fat-soluble vitamin obtained from sun exposure, food or food supplements that requires two hydroxylation in the body to be activated [20]. Vitamin D stimulates the innate immune response and modulates the adaptive immunity reaction due to the presence of vitamin D receptors on macrophages, dendritic cells, B cells and T cells. The vitamin D-inducible response has been reported to be more effective against some pathogens than others [21]. Different studies have demonstrated the positive effects of vitamin D in the prevention of viral respiratory infections and in the immunogenic response to influenza vaccination in children, adults and the elderly (Table 2).

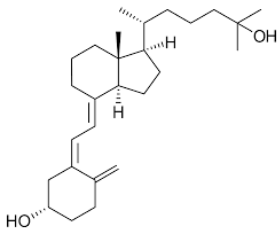
Vitamin D	Role of vitamin D in the immune system	Beneficial effects in viral respiratory infections
	<ul style="list-style-type: none"> Involved in differentiation, proliferation and normal functioning of T cells 	<p>↓ Duration</p>
	<ul style="list-style-type: none"> Increases differentiation of monocytes to macrophages 	<p>↓ Severity</p>
	<ul style="list-style-type: none"> Promotes movement and phagocytic ability of macrophages 	<p>↑ Relief of symptoms</p>
	<ul style="list-style-type: none"> Increases superoxide synthesis 	<p>Preventive effect</p>
	<ul style="list-style-type: none"> Reduces the expression of pro-inflammatory cytokines 	
	<ul style="list-style-type: none"> Maintenance of structural and functional integrity of mucosal cells in innate barriers 	<p>↑ Immunogenic response to specific strains after influenza vaccination</p>
<ul style="list-style-type: none"> Stimulatory effects in innate immunity 		

Table 2: Vitamin D function in the immune system and beneficial effects in respiratory viral infections.

A recent systematic review of the literature on the association between micronutrients deficiency and acute respiratory infections in healthy adults suggested that, compared to other micronutrients, only low levels of vitamin D were associated to longer lasting acute infections of the upper respiratory tract, such as common cold [22]. Low levels of vitamin D have also been associated with a significantly high risk of viral respiratory infections, intensive care unit admission and invasive mechanical ventilation in the paediatric population [23]. Adults with vitamin D deficiency (serum 25(OH)D levels < 20 ng/mL) have been found to be at a significantly increased risk of

community-acquired pneumonia (odds ratio (OR) = 1.64; 95% CI: 1.00; 2.67) [24] while maintenance of a 25-hydroxyvitamin D serum concentration of 38 ng/ml or higher should significantly reduce the incidence and the burden of acute viral respiratory tract infections, at least during the fall and winter in temperate zones. These findings support the potential benefits of vitamin D supplementation in reducing the incidence and severity of specific viral infections, including influenza, in the general population and in subpopulations with lower 25-hydroxyvitamin D concentrations, such as pregnant women, dark skinned individuals, and the obese [25].

Supplementation with vitamin D has been associated with a significant reduction of the risk for developing acute respiratory tract infections in general ($p < 0.0001$) as well as with less ill days [25]. A reduction of influenza infections may reach 50% depending on the dose of vitamin D used [26]. However, improvement of the immunogenic response with production of antibodies in response to influenza vaccination may be dependent on the infecting influenza virus strains, also in the elderly [27].

In patients with recurrent URIs, the common symptoms of cold improved ($p = 0.034$) and significantly less job absenteeism was observed in the group supplemented with vitamin D compared to placebo (14.3% and 47.8%, respectively; $p = 0.038$) [28]. Similarly, in patients with inflammatory bowel disease ($n = 223$), supplementation with vitamin D has been related to a significantly lower incidence of URIs ($p = 0.042$) [29].

A recent meta-analysis has also suggested an important protective role of vitamin D in the prevention of acute viral infections in children [30]. Vitamin D3 supplementation in healthy children has been associated with a lower risk of URIs [31]; no higher doses above the usually recommended ones may be necessary [26].

Other vitamins: Vitamin A and group B vitamins

Research studies have demonstrated that retinoic acid which is a biologically active form of vitamin A has an essential role in mucosal homeostasis, controlling tolerance and immunity in these tissues with non-lymphoid support. Its pleiotropic roles in mucosal immunity includes educating mucosal dendritic cells, differentiation of lymphocyte lineages and imprinting them with mucosal-homing properties as well as in regulating tolerance and immunity by modulating the adaptive Th1-Th2 cell response. Vitamin A also regulates homeostasis at the mucosal surface through influencing a novel lymphocyte subpopulation, the innate lymphoid cells. Vitamin A status also conditions the composition of the intestinal microbiota that regulates intestinal homeostasis and mucosal immune response [32]. Some evidence suggests that vitamin A supplementation helps to relieve clinical symptoms and signs and shorten the length of hospital stay without increasing the incidence rates of adverse reactions in the treatment of pneumonia in children [33]. Also, in non-measles pneumonia in children vitamin A has been associated with a 39% reduction in antibiotic first-line failure (OR 0.65; 95% CI: 0.42; 1.01) and with a significant reduction in the recurrent rate of bronchopneumonia (OR 0.12; 95% CI: 0.03; 0.46) [34].

Vitamin B12 status and supplementation is commonly associated with outcomes in pregnancy and infancy, but much less is known about its effects on immune function. It has been found that Vitamin B12 supplementation throughout pregnancy and 3-month postpartum along with iron and folate significantly increased pandemic influenza A vaccine-specific IgA responses in plasma and colostrum in mothers and reduced the proportion of infants with elevated alpha-1-acid glycoprotein and C-reactive protein which alleviates inflammatory responses compared with placebo [35].

Oligoelements: zinc and selenium

Zinc is a trace element that plays an important role in the regulation of the immune response, in T-cell mediated functions. In viral URIs, zinc inhibits viral replication, intracellular adhesion and enhances the innate immune response at the mucosal surface (Table 3) [36]. The global prevalence of zinc deficiency is estimated to range from 17% to 20% with the vast majority occurring in developing countries of Africa and Asia. Although significantly less common in high-income nations, zinc deficiency occurs most frequently in the elderly, vegans/vegetarians, and individuals with chronic diseases such as liver cirrhosis or inflammatory bowel disease [37].

Zinc supplements in children and adults have been related to a decrease in the incidence and duration of symptoms and signs of common cold [10,38]. In nursing homes, normal serum zinc concentrations have been associated with lower rates and shorter duration of pneumonia in the elderly [39]. However, an observational study showed that 29% of nursing homes residents (≥ 65 years) had low serum zinc levels ($< 70 \mu\text{g/dL}$) despite supplementation with 7 mg/day of zinc sulphate over a period of 1 year. All-cause mortality was 39% lower (RR, 0.61; 95% CI, 0.37 - 1) in those with normal ($\geq 70 \mu\text{g/dL}$) versus low ($< 70 \mu\text{g/dL}$) preintervention serum zinc concentrations ($p = 0.049$). These findings suggest that zinc may play a crucial role in influencing all-cause mortality in the elderly, beyond respiratory infections [40].

Selenium is an essential oligoelement that modulates the immune system, vital metabolic pathways and the antioxidant defence of the human organism. Selenium deficiency reduces T cells proliferation, lymphocytes mediated toxicity and natural killer cells activity [41] (Table 3).

In adults, high dose of selenium have been related to increase activity of glutathione peroxidase that may imply greater chances for a fast recovery from ventilated pneumonia [42] while in children symptoms and signs of respiratory syncytial virus infection were quickly relieved [43].

Selenium has shown a form- and dose-dependent immunogenic response to influenza vaccination in the elderly. It increases T cell proliferation, but without differences in flu virus-specific antibodies suggesting a beneficial effect on the general immune response but not in increasing the immunogenicity after vaccination [44].

Nutrient	Role of zinc and selenium in the immune system	Beneficial effects in viral respiratory infections
Zinc [10,36,38,39]	<ul style="list-style-type: none"> • Modulates T-cell function • \uparrow Immune response at the mucosal surface • Inhibition of the viral replication 	\downarrow Incidence, in adults and elderly
		\downarrow Symptoms
		\downarrow Duration
		\downarrow School absence
Selenium [41-44]	<ul style="list-style-type: none"> • \uparrow Proliferation of T-cells • \uparrow Activity of natural killer cells • \uparrow Antioxidant activity 	\uparrow Recovery
		\uparrow T cell proliferation after Influenza vaccine

Table 3: Zinc and selenium function in the immune system and beneficial effects in respiratory viral infections [36,41].

Zinc and selenium can be combined. In a randomized, double-blind, placebo-controlled clinical trial ($n = 81$), institutionalized elderly (> 65 years) had a significant decrease in the mean number of respiratory infections during a 2-year period of supplementation with micronutrients containing 20 mg of zinc sulphate and 100 μg of selenium sulphide. In another, larger ($n = 725$), randomized, double-blind, placebo-controlled intervention study, low-dose zinc and selenium supplementation significantly increased the humoral response in institutionalized elderly subjects (aged 65 - 103 years) after vaccination. The number of subjects without respiratory infections during the studies period was also higher in the groups that received trace elements over 2 years suggesting a potential protective effect [40].

Probiotics

Probiotics are defined as live microorganisms that when being administered in appropriate doses, confer a benefit to the health of the host [45]. The two most common types are *Lactobacilli* and *Bifidobacteria*, which are generally consumed in fermented foods or dietary supplements. Probiotics have an influence on the gut mucosa by balancing the local microbiota by inhibiting the growth of pathogenic microorganisms and a significant effect on the functionality of the immune system by interacting with dendritic cells, epithelial cells, T regulatory cells, lymphocytes, natural killer cells and B cells depending on the bacterial strain [63,64]. Evidence shows that probiotics can be beneficial in viral respiratory infections, decreasing the risk or duration of the infection in children, adults, elderly and specific population groups. Probiotics may also have a role in the immune response to influenza vaccination (Table 4) [64].

Probiotics	Role of probiotics in the immune system	Beneficial effects in viral respiratory infections	
<i>Lactobacilli</i>	<ul style="list-style-type: none"> • Increase of antibody expression 	↓ URI episodes	
		↓ Symptoms	
<i>Bifidobacterium</i>	<ul style="list-style-type: none"> • Increase Treg cells • Activation of natural killer cells • Induction of IgA, important in host defence against mucosal transmitted pathogens • Reduces the expression of pro-inflammatory cytokines • Promotion of phagocytosis 	↓ Duration	
		↑ Preventive effect	
		↑ Immunogenic response to specific strains after influenza vaccination	
IgA: Immunoglobulin A; Treg: Regulatory T Cells; URI: Upper Respiratory Tract Infection			

Table 4: Probiotics function in the immune system and beneficial effects in respiratory viral infections [64].

In children, the most studied probiotics (*Lactobacillus rhamnosus L. casei* and *L. fermentum*) reduced the risk of URIs as well as the duration and recurrence of URIs. In healthy adults, the use of probiotics decreased the duration and severity of URIs symptoms. In the elderly, the supplementation with *L. casei* and a combination of different strains of probiotics reduced the duration of the infection [48].

Recent studies have provided evidence for specific population groups. For instance, in endurance athletes, the use of *Lactobacillus casei* has benefited their overall immune status [49] while in elite athletes, *Lactobacillus helveticus* has decreased the duration and the number of symptoms of viral URIs (50). The use of probiotics amongst military conscripts has also been associated with a reduction of symptoms of respiratory infections [51]. In nursing homes, the use of *Lactobacillus rhamnosus* supplementation has been related to a smaller number of laboratory confirmed viral respiratory infections (HR = 0.65, 95% CI: 0.32; 1.31) [52].

Probiotics, *Bacillus subtilis* and *Enterococcus faecalis*, have shown the potential to prevent ventilator-associated pneumonia (VAP) in critically ill adult patients who were expected to receive mechanical ventilation for ≥ 48h with a significantly longer mean time to VAP development, a smaller proportion of patients with acquisition of gastric colonization of potentially pathogenic microorganisms (PPMOs) [53]. These findings suggest that the use of the probiotic bacteria *B. subtilis* and *E. faecalis* may be an effective and safe means for preventing VAP and the acquisition of PPMO colonization in the stomach in critically ill adults. Furthermore, certain combinations of probiotics including *Bifidobacterium longum* + *Lactobacillus bulgaricus* + *Streptococcus thermophiles* and *Lactobacillus rhamnosus* have been found to be highly efficacious and superior to placebo in preventing VAP (66%) also reducing hospital mortality and intensive care unit mortality [54].

In 2013, during the avian-origin influenza A (H7N9) virus that spread among humans in Eastern China, it was suggested that H7N9 infection might decrease intestinal microbial diversity and species richness in humans, and that prophylactic treatment with antibiotics and probiotics for secondary infection is important. It was found that *B. subtilis* and *E. faecium* appeared to reduce and/or ameliorate secondary infections with patients displaying a trend towards increasing diversity and evenness [55]. Noticeable, most recent evidence has confirmed that some patients with COVID-19 showed intestinal microbial dysbiosis with decreased probiotics such as *Lactobacillus* and *Bifidobacterium* indicating the need for regularly assessing the nutritional and gastrointestinal function in all patients at risk. The application of prebiotics and/or probiotics in this population has been suggested to regulate the balance of intestinal microbiota and reduce the risk of secondary infection due to bacterial translocation [56].

Two meta-analysis published in 2017 and 2018, respectively, suggested that probiotics are effective in elevating immunogenicity in adults inoculated with influenza vaccines [74,75]. Patients presented higher seroprotection and seroconversion rates against the most common influenza strains (H1N1, H3N1 and B). The duration of the usage of probiotics had a linear and direct effect on the stimulation of the immune system by the vaccine [58].

Other diet elements: Quercetin and N-acetylcysteine

Other important elements of the diet such as flavonoids or amino acids have shown beneficial effects on prevention of URTIs in limited clinical studies (Table 5). Quercetin is a flavonoid present in a variety of fruits and vegetables. Flavonoids have been proposed to reduce the incidence of URTIs because of their antiviral, anti-inflammatory, cytotoxic and antioxidant effect [59]. Different studies have provided evidence about the reduction of URTIs in high intensity athletes ($p = 0.004$) by supplementation with quercetin [60,61]. N-acetylcysteine (NAC) has well described antioxidant, anti-inflammatory and mucolytic properties. NAC is, also, a precursor of glutathione, a tripeptide with antioxidant and anti-inflammatory effects [62]. Evidence shows that NAC improves oxidative stress in patients with community acquired pneumonia reducing the oxidative and inflammatory damage in pneumonia patients [63].

	Role in the immune system	Beneficial effects in common cold and influenza
Quercetin (flavonoids) [59,60]	<ul style="list-style-type: none"> • Antiviral • Cytotoxic 	↑ Preventive effect ($p = 0.004$)
N-acetylcysteine [63]	<ul style="list-style-type: none"> • Antioxidant • Anti-inflammatory 	↓ Oxidative damage caused in pneumonia

Table 5: Function quercetin and N-acetylcysteine in the immune system and their beneficial effects in respiratory viral infections [64].

Herbs and botanical extracts

Several authors argue that herbal and botanical extracts have long been used to treat and prevent viral respiratory infections and the use of these herbs has become more frequent when effective treatments or vaccines are unavailable [65,66]. Some preliminary data support the notion that the benefit of most of these herbs derive from their built-in immune-stimulating and inflammation-modulating effects meaning that they can help prevent immune overreaction to viral respiratory infections while still helping the immune system cope better with the infections [65].

Herbs and botanical extracts have mostly been studied in influenza virus infections and common cold (Table 6) [64]. *Astragalus* has a preventive effect decreasing the incidence rates of URIs [67]. Elderberry extracts enhance the immune function due to the polyphenols

they contain, and help reducing the number of symptoms and days missed at work or school in healthy adults with URIs [68]. Lactoferrin is a glycoprotein with antiviral activity that is present in exocrine secretions, like milk that has been related to a reduction in the incidence of common cold [69]. *Andrographis paniculata*, a native Indian plant with immunostimulatory activity has shown to decrease URIs symptoms [70]. A seaweed extract has demonstrated to increase influenza vaccine immunogenicity in healthy adults and the elderly.

Herbs and extracts	Role in the immune system	Beneficial effects in common cold and influenza
Astragalus [67,73]	<ul style="list-style-type: none"> • ↑ white blood cells • ↑ Macrophage production • ↑ Natural killer cells activity • ↑ T-cell production • ↑ production of interleukins 	↑ Preventive effect
Elderberry (polyphenols) [68,74,75]	<ul style="list-style-type: none"> • ↑ T cell proliferation • ↑ Functional immunity (barrier protection) 	↓ Number of symptoms (p = 0.031) ↓ Days missed at work/school (p = 0.329)
Lactoferrin [69]	<ul style="list-style-type: none"> • Antiviral activity • Inhibits cytopathic effect of virus 	↓ Symptoms ↓ Incidence
Andrographis [70,76]	<ul style="list-style-type: none"> • Immunostimulatory activity 	↓ Symptoms (p < 0.05)
Mekabu fucoidan (sulphated polysaccharide extracted from seaweed) [71]	<ul style="list-style-type: none"> • ↑ Antibodies • ↑ Natural killer cell activity 	↑ Immunogenicity after administration of Influenza vaccine in the elderly
CI: Confidence Interval; RR: Relative Risk		

Table 6: Function of herbs and extracts in the immune system and their beneficial effects in respiratory viral infections [64].

Conclusion

Decreasing the burden of respiratory viral infections is of high importance provided their morbid and fatal potential, especially in high risk populations. There is substantial evidence supporting the notion that micronutrients are crucial for a correct function of the immune system. Overall, vitamins C and D as well as zinc, selenium and probiotics are at the cornerstone for strengthening the immune response to viral respiratory infections. Vitamin C and D are fundamental for ameliorating the burden of acute URIs and pneumonia, particularly in high risk individuals and in patients who have low vitamins C and D plasma levels. Probiotics are essential to guarantee the diversity and good balance of the microbiota of epitheliums with a potentially significant role in the recovery of critically ill patients after infections of the upper and lower respiratory tract. Herbs and botanical extracts help diminishing the number and length of symptoms. All elements of the diet reviewed exert some immunomodulatory effect that improves the response to anti-viral vaccination. More research is needed to precise the role of micronutrients and other common elements of the diet to inform their most appropriate and correct use as well as the health outcomes to be expected.

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