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## Narrative Review

## Can an anti-inflammatory diet be effective in preventing or treating viral respiratory diseases? A systematic narrative review

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## SUMMARY

Respiratory Viruses infections (RVI) such as rhinovirus, coronavirus, influenza virus, and adenovirus affect the respiratory and the immune systems. The role of nutrition in the respiratory and immune systems has been studied in some studies, and its importance is undeniable. In addition, one of the key findings in this disease is high inflammation that affects almost all patients. This systematic narrative review aims to answer the question, “Can an anti-inflammatory diet be effective in preventing or treating viral respiratory diseases?” A systematic review search was used for the articles extraction. All studies published in English from 1999 to 2020 investigating dietary inflammatory conditions and RVI were included. Food items with anti-inflammatory properties were selected based on the definition of the dietary inflammatory index (DII). We used Google Scholar, Pub Med, Scopus, Web of Science, Springer, Science Direct, Directory of Open Access Journals, Elsevier, Taylor and Francis, ProQuest, EBSCO, MEDLINE, and SciELO databases for extracting articles. Keywords were restricted by DII. Based on DII, food items/nutrients are involved in inflammation, some of which have anti-inflammatory and some inflammatory properties. Some foods/nutrients, in addition to their anti-inflammatory properties, have antioxidant, antiviral, and immune-enhancing properties. Considering the immune system's involvement, increased inflammation, and involvement of the pulmonary system in RVI and the remarkable role of the anti-inflammatory foods for counteracting them, it is recommended to use a predominantly anti-inflammatory diet along with prevention/control and treatment protocols.

An anti-inflammatory diet (based on DII) includes turmeric, ginger, garlic, onions, saffron, dietary vitamin C, vitamin D, zinc, and omega-3 are recommended to reduce infection symptoms and duration.

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## 1. Introduction

Due to the Respiratory Viruses Infections (RVI) nature, viral pandemics can spread and engage many individuals worldwide [1]. The spread of RVI is a severe risk to human health and life. So many people die each year from emerging RVI, and many are involved [1]. Therefore, there is a considerable cost to the country's health care system and economy to prevent the spread and control of the disease [1]. The Coronavirus Disease 2019 (Covid-19) is one of the emerging pandemics created by the coronaviruses family [2]. Annually, millions are infected, and thousands die from RVI [3]. The RVI, such as Covid-19 and severe acute

respiratory syndrome-related coronavirus (SARSr-CoV), belongs to the coronaviruses' family and recently caused pandemic [4,5]. With the advent of the Covid-19, which has more expansion power than its family [4], global concerns have increased, and the World Health Organization (WHO) has described the international alert level as very high [6].

Along with other topics, what appears to be meaningful and controversial is nutrition/diet/food items in the prevention, control, and even treatment of RVI. In this regard, nutrition plays an undeniable and crucial role in the immune system [7–9]. The intake of certain micronutrients, such as vitamin (vit) C [10,11], zinc (Zn) [12], and vit D [13], strengthens the immune system and can protect the body against diseases. Besides, getting enough protein as a marker of immune system compounds can be beneficial [14,15]. Previous epidemics and numerous studies on the relationship between the immune system and nutrition have yielded acceptable and

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significant results [16,17]. Studies show that the intake of micronutrients such as Zn [18,19] and vit D [20,21] has been implicated in the prevention, control, and treatment of some RVI. Some studies have found an insignificant association and some of them raised issues such as the received dose or the specific micronutrient deficiency or micronutrient intake through supplementation or diet [22,23]. However, studies have shown that people who have a deficiency of a particular micronutrient such as vit D [20,21] and Zn [18,19] will benefit from taking the supplement. It is sufficient to get nutrients through the diet at the recommended levels. Therefore, nutrient-rich food intake is the priority to strengthen the immune system, not supplements [24]. However, it is fundamental to pay attention to the whole diet so that the synergistic effects are far more critical than the intake of a single nutrient or food item [25,26]. The relationship between the anti-inflammatory diet and the incidence and risk of some diseases has been well demonstrated [27,28]. According to the results of more than 10,000 studies, 45 food items are involved in dietary inflammation, some of which increase or decrease inflammation [27–29]. The critical issue about the foods on this list is that in addition to their anti-inflammatory properties, they also can play an essential role in boosting the immune system, improving lung function, and detoxification of oxidants [27–29]. Therefore, these properties can prevent/control or even treat RVI, which is worth considering.

In this study, we aimed to conduct a systematic narrative review and answer this question; can an anti-inflammatory diet effectively prevent or treat RVI?

## 2. Methods

A systematic review search was used for the articles extraction. All studies published in English from October 1999 to September 2020, having dietary items/inflammatory conditions related to RVI, were included. Two reviewers other than authors (who worked independently) initially assessed the title/abstract of 401 papers, and 66 papers were selected for future assessments. After full review and consideration of the inclusion and exclusion criteria, we used 31 articles.

In this regard, the question was designed: “Can an anti-inflammatory diet be effective in preventing or treating RVI?” According to the research question and study protocol, we used Pub Med, Google Scholar, Web of Science, Science Direct, Taylor and Francis, Elsevier, Springer, Directory of Open Access Journals, ProQuest, Scopus, EBSCO, SciELO, and MEDLINE databases for extracting articles. Food items with anti-inflammatory properties were selected based on the definition of the dietary inflammatory index (DII) [30].

### 2.1. Search keywords and strategy

“Virus AND diet”; “virus AND inflammation”; “virus AND vitamins”; “virus AND minerals”; “virus AND dietary inflammation”; “virus AND diet AND inflammation”; “virus AND diet therapy”; “virus AND nutrition”; “virus AND nutrition therapy”; “virus AND nutrition AND inflammation”; “virus AND CRP”; “virus AND IL”; “virus AND TNF”; “virus AND vitamin C”; “virus AND acid ascorbic”; “virus AND zinc”; “virus AND vitamin D”; “virus AND calcitriol”; “virus AND vitamin E”; “virus AND tocopherol”; “virus AND vitamin A”; “virus AND retinol”; “virus AND beta-carotene”; “virus AND carotenoids”; “virus AND herbal”; “virus AND garlic”; “virus AND allicin”; “virus AND ginger”; “virus AND onions”; “virus AND fats”; “virus AND fatty acids”; “virus AND w3”; “virus AND w6”; “virus AND w9”; “virus AND MUFA”; “virus AND PUFA”; “virus AND monounsaturated

fatty acids”; “virus AND polyunsaturated fatty acids”; “virus AND linoleic”; “virus AND oleic”; “virus AND linolenic”; “virus AND ginger”; “virus AND oxidant”; “virus AND antioxidant”; “virus AND antiviral”; “virus AND antiviral foods”; “virus AND antiviral nutrients”; “virus AND antiviral herbs”; “virus AND turmeric”; “virus AND curcumin”; “virus AND ...”.

In addition, we use advanced research protocols such as [ti] [author] [Virus\*] [viral\*]; “viral\*[ti] AND diet\*[ti]”; “virus\*[ti] AND inflammation\*[ti]”.

All searches were done by replacing “virus” with “viral”; “respiratory viral”; “respiratory viral disease”; “viral disease”; “viral infection,” “HRSV”; “HPIV”; “HRV”; “ADV”; “HCoV,” “SARS-CoV”; “HMPV”; “HBoV.”

The results for different types of food items were limited to the list of foods in the DII. Articles related to food items that were not in the DII list were excluded.

## 3. Based on systematic research, the following are some crucial compounds of the anti-inflammatory diet (based on the DII) and describe their role in preventing/controlling, or treatment of RVI and improving lung and/or immune function

### 3.1. Food items

#### 3.1.1. Turmeric

One of the influential elements in the anti-inflammatory diet is turmeric, used as spices in various foods [27,28]. The fundamental ingredient in turmeric is a polyphenol called curcumin (difluoroethyl methane) [31]. In addition to curcumin, many nutrients in turmeric have beneficial effects on human health [31]. The anti-inflammatory properties of curcumin are equivalent to the effect of steroidal and non-steroidal drugs such as phenylbutazone [32]. This drug reveals its anti-inflammatory effect by inhibiting the biosynthesis of prostaglandins (PGs) [32]. As well as anti-inflammatory properties, curcumin shows some antiviral effects [33]. Inosine-5'-monophosphate dehydrogenase enzyme due to rate-limiting activity in the biosynthesis of guanine-nucleotides is proposed as a therapeutic object for antiviral compounds [33]. Between several polyphenols, curcumin as an Inosine-5'-monophosphate dehydrogenase inhibitor, either noncompetitive or competitive, is proposed as a potent antiviral compound [33,34]. The survey of the bio-conjugates of curcumin such as di-O-tryptophanylphenylalanine, di-O-decanoyl, di-O-pamitoyl, di-O-bis-( $\gamma,\gamma$ ) foyl, C4-ethyl-O- $\gamma$ -folyl, and 4-O-ethyl-O- $\gamma$ -folyl, facing a diversity of viruses including parainfluenza virus type III, feline infectious peritonitis virus, herpes simplex virus, and respiratory syncytial virus showed the strong antiviral properties of curcumin and its bio-conjugates facing various viral pathogens [35,36]. Besides, di-O tryptophanylphenylalanine curcumin and di-O-decanoyl curcumin showed remarkable antiviral properties against RVI. In addition, curcumin showed a significant anti-influenza activity [35,36]. These studies highlight the critical role of turmeric in the fight against RVI.

On the other hand, curcumin plays a significant role in the immune system [37]. Curcumin remarkably inhibits cytokine gene expression at mRNA and/or protein biosynthesis levels, but NF- $\kappa$ B interferes only with the lower dose of curcumin [37]. In addition, curcumin makes a significant reduction in the inflammatory infiltrate and increases collagen content and fibroblastic cell numbers [37].

According to what has been said, turmeric is an essential part of an anti-inflammatory diet with antiviral properties. It may play

a role in improving lung function and liver detoxification in RVI [38].

### 3.1.2. Ginger

Another important component of the anti-inflammatory diet is ginger, which has shown significant anti-inflammatory properties [39]. Ginger is a spice or medicinal herb that belongs to the curcumin family and is the root of *Zingiber Officinale* (ZO) [40]. A study has shown that fresh ZO was dose-dependently effective against HRSV in HEp-2 and A549 cells [40]. Another study stated that ginger oil intake results in the reduction of titer HA [41]. Interestingly, ginger oil shows anti-viral activity revealed HA [42]. This study's conclusion proved that ginger oil is the best anti-viral activity concentration [39,42]. Another important effect of ginger is its role in reducing lung inflammation. Studies have shown that ginger reduced the production of PGE2 and TXA2 [41,42]. In addition, ginger reduced myeloperoxidase activity and the number of cells in the bronchoalveolar [42]. The results show that ginger has an anti-inflammatory effect on the lung [41]. Based on these studies and considering the anti-inflammatory, antioxidant, and antiviral role, it can be concluded that ginger can be placed in the food group to counteract the inflammation caused by RVI.

### 3.1.3. Garlic

Garlic is an essential food item that has a crucial role in RVI and has antioxidant and cholesterol-lowering, and anti-inflammatory effects [43]. One of the most important results that can be mentioned on garlic's benefits is improving respiratory infections [44]. Studies have examined the effect of garlic on respiratory diseases and observed significant results [45,46]. Other garlic uses include treating fever, cough, headache, abdominal pain, sinus congestion, asthma, bronchitis, and shortness of breath [44]. Garlic is high in folic acid, vit C, calcium, iron, magnesium, potassium, and a small amount of Zn and vit B2, B1, and B3 [44,47]. Garlic is a potent antifungal, antiviral, and natural antibiotic that contains potassium and germanium, which improves health [47]. Germanium can neutralize positive ions, facilitate blood flow, increase energy levels in the body, and relieve pain and cramps [47]. One of the garlic's strategic ingredients is allicin, a light yellow compound that produces garlic's unique aroma. One review study reported that allicin could prevent or control the common cold [48]. This review study, which included interventional and cohort studies, concluded that garlic or its extracts also could play an essential role in RVI [48].

However, in comparison with garlic's antibacterial action, very little work has been done to exam antiviral effects. Organosulfur compounds like diallyl trisulfide, allicin, and ajoene are the main chemicals that impart antiviral properties to garlic [48]. According to the studies, garlic extracts can pass through the cell's phospholipid membrane and inhibit virus proliferation [49,50]. Several studies have shown that garlic demonstrates activity versus influenza, cytomegalovirus, rhinovirus, herpes simplex virus-I and II, viral pneumonia, and rotavirus [49–51]. Any other way, several articles have surveyed the aspect of garlic or its products in strengthening the immune system [52,53]. Also, garlic can block the biosynthesis of inflammatory markers such as Interleukin (IL)-6 and Tumor necrosis factor (TNF)- $\alpha$  [54]. Garlic extract has the property to change the NF- $\kappa$ B transcription and DNA binding activity [54]. It can also block the expression of NF- $\kappa$ B-mediated pro-inflammatory target genes [54]. Studies proposed that garlic may be a promising nominee as a biological immune accountability modulator, retain the immune system's homeostasis, agitate required actions, and repress dispensable ones [55]. A variety of

immunomodulatory effects have been surveyed in different garlic extracts [55].

### 3.1.4. Onion

The onion has phytochemical compounds such as phenols, which are now undergoing fundamental research to determine their possible effects on human health [44,56]. Like garlic, onion is one of the constituents of the anti-inflammatory diet, which in addition to its anti-inflammatory properties has antioxidant, antibacterial, antiviral, and immune-enhancing properties [56]. Organosulfur compounds such as quercetin and allicin are related to the deterrence of VIs [57,58]. These compounds can prevent virus attachment to host cells, change transcription and translation of the virus genome in the host cell and affect viral aggregation [57,58]. As an anti-inflammatory compound, quercetin can affect the Enterovirus and Influenza virus's entry and enclosure on the host cell [57,58]. Quercetin can inhibit RNA polymerase that is necessary for viral proliferation. Quercetin also affects how a virus changes signaling pathways in the host cell [57,58]. Some studies that surveyed the antiviral effect of onion recommend using these plants as a safe alternative to prevent RVI. One of the crucial concerns in treating RVI is developing resistance in the virus against antiviral drugs. The high mutation rate of viral RNA polymerase enhances this resistance in viruses with an RNA genome. Studies have shown an inhibitory effect of quercetin on viral proliferation [57,58]. For instance, quercetin has been verified to inhibit poliovirus RNA's translation [57,58]. In this regard, SARS-CoV protease, required for the SARS virus's proliferation, was inhibited by the quercetin [59,60]. Besides, quercetin increases Zn uptake, which can inhibit RNA-polymerase [59,60]. The presence of quercetin increases the phosphorylation of eIF2 in response to viral infection and thereby prevents viral proliferation. Therefore, quercetin's application efficiently enhances the host cells' immune response [59,60]. Quercetin has a strong probability of inhibiting a new progeny virus's convocation in the host cells [61]. Mechanism of quercetin in host cell: VIs includes a. Attachment of virus on the host cell membrane, b. Virus entry in the host cell, e. Reverse transcription, d. Replication of virus genetic material, f. transcription, h. Translation and g. Viral assembly [49]. Quercetin can prevent attachment of virus-like Influenza virus, Ebola, and Enterovirus to hosts cells [49]. As quercetin plays an important role in imparting antiviral property to the onion, similarly, allicin is the chemical present in garlic, which acts against the virus [49].

On the other hand, studies have shown the protective effects of onions against oxidants in the lung [56]. Studies showed that onion extract remarkably lowered oxidant markers like Ig-E and IL-4 and could have remedial potential to be used versus pulmonary difficulties through antioxidant and immune-modulatory procedures [56]. Given the anti-inflammatory, antioxidant, antiviral, and beneficial effects on lung function, it can be concluded that onions can also be considered as an anti-inflammatory component of the anti-inflammatory diet.

## 3.2. Micronutrients

In the anti-inflammatory diet (based on DII), some minerals and vitamins play an essential role. Below we examine the role of the most important ones of them in reducing inflammation, antioxidant and antiviral effects, and other beneficial effects in RVI:

### 3.2.1. Vitamin C

Traditionally, vit C has been used to prevent, control, and even treat RVI [62]. Vit C supplements have been previously recommended for the common cold and flu [62]. Given the number of pros and cons, it is difficult to conclude whether vitamin C

supplements help these cases. However, the important point is that dietary vit C can help, but whether its supplementation is needed or not needs further investigation [62]. So getting vit C in the amount that is provided through food is recommended [63]. Major foods containing vit C include citrus fruits, strawberries, and tomatoes, will help fight against RVI [63,64]. Some studies have shown a reverse association between dietary vit C intakes and inflammation indicators, including C - reactive protein (CRP); IL-6, fibrinogen, and coagulation factors VII, VIII, and IX; prothrombin fragments; and thrombin-antithrombin complexes [62–64].

In addition to the anti-inflammatory effects mentioned above, vit C has a significant role in neutralizing the oxidants produced in the body [64]. Inflammatory cytokines and CRP are increased in different stages of RVI and can, thus, be applied as markers for situations that affect primal endothelial activation and inflammation [62–64].

Another effect of vit C is its antiviral activities [65,66]. These effects have been demonstrated by boosting the immune system and directly against RVI [66]. Studies examined the association between VIs and vit C involved poliomyelitis, viral hepatitis, measles, mumps, chickenpox, shingles, infectious mononucleosis, viral encephalitis, and influenza. Vit C has been demonstrated to confronting both DNA- and RNA-containing viruses that infect humans [66]. Vit C caused the inactivation of a wide range of viruses, including herpes simplex, vaccinia, foot-and-mouth disease, rabies, tobacco mosaic, and bacterial viruses [66]. Vit C caused inactivation of the virion-associated enzyme, reverse transcriptase, upon prolonged incubation of virus particles [66]. Vit C, in condensation certain to host cells, participated with a continuous multicycle copy of rhinovirus. In a lymphocytic cell line, most recently infected with human T-cell leukemia virus, vit C was shown to interfere with virus proliferation [66]. Besides its direct antiviral and antioxidant properties, vit C may afford additional protection against RVI by affecting the immune system [62–64]. Studies suggested that lymphoid cells could cumulate vit C to concentrations at least 50 times higher than those present in blood plasma [65,66]. Vit C can influence the motility and chemotaxis of phagocytes [66]. The antioxidant ability of vit C provides cellular protection to phagocytes from oxidative self-damage caused by free radicals without interfering with their formation during the respiratory burst process. Phagocytosis involves the engulfing, ingestion, and destruction of microorganisms by phagocytic leukocytes [66]. The latter include polymorph nuclear neutrophils, eosinophils, and monocytes-macrophages that can ingest and destroy microorganisms [66]. Dietary vit C was also shown to enhance interferon production after stimulation with murine leukemia virus [66]. Vit C also demonstrated enhanced interferon production in mouse and human embryonic fibroblasts [66]. Vit C has been reported to regenerate vit E from the tocopherol free radical [67]. Studies suggest that the main effect of vit C may lie in its impact on vit E levels [67]. Regarding proven antiviral and immunomodulatory effects of vit C, it should have potential value in controlling RVI.

### 3.2.2. Vitamin D

Vit D is one of the most effective vitamins in strengthening the immune system [68], and studies have shown that it can prevent respiratory infections [68–70], especially in the RVI. However, one of the most controversial components of the anti-inflammatory diet is vit D. Because, on the one hand, it has been shown to have anti-inflammatory and immune-enhancing effects. On the other hand, too much long-term intake can cause poisoning, like other fat-soluble vitamins [68]. Another concern about vit D is its high deficiency prevalence in some countries or areas. For example, in Iranian women, the prevalence of vit D deficiency is 75.1%, and in men, 72.1 percent [71], in Hispanic-Americans, 65% and African-

Americans 87% [72,73]. Given the high prevalence of deficiency, vit D supplements appear to be helpful in most areas, or at least in those with high prevalence [74]. Different countries have different protocols to control deficiency. The protocol of the WHO is as follows: In people who have a severe deficiency (serum concentration less than 12 ng/mL) and have a history of vit deficiency in the past year without supplementation, it is recommended to take vit D supplements at a dose of 50,000 IU per week for 6–8 weeks. The daily intake of 800–1000 IU will continue until it reaches the desired level (higher than 50 ng/mL). It is important to note that people who are already taking vit D supplements should continue to take supplements by their treatment protocol. For those with a moderate deficiency (serum concentration of 20–12 ng/mL), a daily intake of 800–1000 IU vit D is recommended that should be continued until it reaches the optimal level (higher than 50 ng/mL). For those with a mild deficiency (serum concentration of 30–30 ng/mL), a daily intake of 800–600 IU vit D is recommended that should be continued until it reaches the optimal level (higher than 50 ng/mL). It should be noted that oral intake of vit D at low doses and more often than injectable or single-dose forms at high doses is more effective in increasing serum levels of vit D.

The mechanisms by which vit D modulates inflammation are multiplex [68,75,76]. Vit D adjusts the innate and adaptive immune systems [77]; the all-over consequence is an alteration from the more inflammatory T-helper1 (Th1)/Th17 respond to the less inflammatory Th2/Treg gnomon [77]. In vitro, these consequences affect the decreased production of pro-inflammatory markers such as TNF- $\alpha$ , IFN- $\gamma$ , IL-12, IL-17, and IL-21 but with increased anti-inflammatory production cytokines such as IL-10 [75,76]. Studies showed that higher vit D is related to decrease condensation of inflammatory indicators proposed that local autocrine production of vit D is binding to genes down-regulating pro-inflammatory cytokines and up-regulating anti-inflammatory ones [75,76]. A review suggests that vit D's effectiveness in lowering inflammation indicators appears to depend mainly on the disease state studied and baseline vit D concentrations. Vit D, in highly inflammatory conditions, found significant beneficial effects [75,76]. Along with anti-inflammatory effects, vit D also affects the immune system and appears to strengthen it [77]. It is broadly considered that all immune cell types can react to vit D [77,78]. More specifically, vit D suggested keeping the activated Th1/Th17 cells in the circulation and blocking them from passing the blood–brain barrier [77–79]. Activation of Th cells by antigen leads to the production of Th subgroups with definite cytokine profiles: Th<sub>1</sub> (IL-2, IFN $\gamma$ , TNF- $\alpha$ ) and Th<sub>2</sub> (IL-3, IL-4, IL-5, IL-10) that respectively support cell-mediated and immunity [79]. There are four potential mechanisms by which vit D can influence T-cell function: a) undeviating effects on T cells mediated via vit D; b) indirect effects on antigen presentation to T cells mediated via localized DC expression of CYP27B1 and intracrine synthesis of vit D; c) undeviating effects of vit D on T cells following synthesis of the active form of vit D by CYP27B1-expressing monocytes or DCs; d) intracranial conversion of 25OHD to 1,25(OH)<sub>2</sub>D by T cells [79].

Given the evidence and attention are given to the immune-enhancing, and anti-inflammatory effects of vit D, one of the essential components of an anti-inflammatory diet to prevent and/or control RVI will probably be vit D.

### 3.2.3. Zinc

Zn is an essential mineral that has potent antioxidant and anti-inflammatory properties [80]. Zn intake from food sources will help strengthen the immune system [81]. The particularly important issue regarding Zn is its crucial role in older adults' immune system, one of the most influential groups at risk for RVI. As mentioned, oxidative stress (OS) is an important, significant determinant

in many chronic diseases [82]. Inflammatory markers such as TNF- $\alpha$  and IL-1 produced by activated monocytes–macrophages generate increased ROS quantities [82]. NF- $\kappa$ B is involved in expressing a wide range of responsive-specific genes and is activated by several stimuli such as cytokines, radiation, and OS [80]. Studies showed that Zn could restrain NF- $\kappa$ B activation [80]. A Zn-finger transactivating factor binds to DNA producing A20 protein, which inhibits TNF- $\alpha$ -induced NF- $\kappa$ B activation. A20 plays an important role in reducing IL-1 $\beta$ - and TNF- $\alpha$ -induced NF- $\kappa$ B activation [82]. Zn impaired situation undergoes OS and DNA damage, and their ability to repair this damage is also compromised [82,83]. Zn may modulate OS in cells by some conceivable biochemical mechanisms. One study showed, Zn modulates gene expression of some inflammatory cytokines such as TNF- $\alpha$  and IL-1 $\beta$ , which can produce ROS, and this is a further mechanism by which Zn probably operating as an AO [80]. Zn is an essential micronutrient for normal evolution and cell-mediating innate immunity, neutrophils, and natural killer cells [80]. Macrophages, phagocytosis, intracellular killing, cytokine production, and T and B cells' development and activity are also affected by Zn deficiency [80]. Zn is required for DNA biosynthesis and RNA transcription, cell division, and cell function [80]. Zn deficiency adversely affects cytokines' production and activity, the immune system's primary markers [80]. Zn acts as an antioxidant and sustains cell membranes [84]. Studies showed that the production of INF- $\gamma$  was reduced since the generation of Th<sub>2</sub> cytokines IL-4, IL-6, and IL-10 were not influence due to Zn deficiency [80]. Zn deficiency declined NK cell functions and affected a reduction in the proportion of CD8+ CD73+ T cells [80,84]. Zn's antioxidant properties have been demonstrated [84] and, for the most part, appear to be independent of Zn metalloenzyme activity. Therefore, according to the study's results, Zn can be included as an anti-inflammatory compound in the anti-inflammatory diet to fight RVI.

### 3.2.4. Omega 3 fatty acids

Omega 3 fatty acids ( $\omega$ -3 FAs), mainly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), can quell inflammation and have a remarkable role in divers inflammatory diseases [85]. The  $\omega$ -3 FAs can inhibit the generation of inflammatory markers, such as IL-1 $\beta$ . On the other hand, DHA can suppress LPS-induced NF- $\kappa$ B activation and TNF- $\alpha$  generation. The  $\omega$ -3 FAs suppress NLRP3 or NLRP1b inflammasome function [86]. NLRP3 inflammasome can be activated by pathogen-associated molecular patterns and danger-associated molecular patterns [86]. DHA inhibited caspase-1 cleavage and IL-1 $\beta$  production started by all surveyed agonists, such as MSU, Alum, R837, and ATP, alike to nigericin [86]. Studies proposed that  $\omega$ -3 FAs are potent and comprehensive suppressors of NLRP3 inflammasome activation [86]. The  $\omega$ -3 FAs can signal through GPRs to inhibit NLRP3 inflammasome activation and explain the enhanced inflammation [86]. Regarding  $\omega$ -3 FAs intake, one of the issues discussed is the ratio of  $\omega$ -6 FAs to  $\omega$ -3 FAs [87]. Being high or low in this ratio can impair the  $\omega$ -3 FAs' protective effects [88]. Also, the favorable property of  $\omega$ -3 FAs on lung function has been shown in numerous studies [89–91]. In some lung diseases such as cystic fibrosis and asthma, its beneficial effects have been well demonstrated [91]. The  $\omega$ -3 FAs, EPA, and/or one of the vegetable sources of omega-3 fatty acids, alpha-linolenic acid (LNA), increases the levels of EPA in the phospholipids of cell membranes by up to 10 fold and reduces the synthesis of the pro-inflammatory cytokines IL-1 and TNF [89–91]. In asthmatic adolescents, a moderate fish oil of 1.2 g/day of  $\omega$ -3 FAs and comparatively negligible adjustment to the diet-induced a fivefold boost in blood EPA [92].

Another notable effect of omega-3s is their role in pulmonary tissue remodeling, which is also important in RVI. A recent survey

provided evidence for NF- $\kappa$ B activation in severely underweight COPD patients in muscle biopsies, making it a potentially interesting target for modulation by PUFA [93]. PUFA intake has a protective effect on COPD development, decreasing risk dose-dependently and increasing lung function [39]. PUFA as PPAR activators promotes circulating fatty acids by cells through the lipoprotein lipase gene's upregulation. In addition, PPARs control mitochondrial beta-oxidation and fatty acid import [39]. It is possible that the increase in exercise burden persuaded by PUFA could be associated with a PUFA-induced activation of PPAR, growing fatty acid accessibility, and oxidation. This potential increase in oxidative capacity might be related to changes in fiber types [39].

Based on the evidence presented, long-chain fatty acids can be a good option for improving pulmonary function in patients with RVI.

## 4. Discussion

With the outbreak of the Covid-19 that is associated with immune and pulmonary involvement and has affected many countries, the need to strengthen the immune system and improve pulmonary function is strongly felt. The role of micronutrients and food items has been well demonstrated to enhance the immune system. The role of some micronutrients in improving lung function and antioxidant activity has been shown in many studies. The part of anti-inflammatory foods has also been multiplied, as RVI causes a highly inflammatory status in the patient's body and elevated inflammatory markers such as CRP. The foods and micronutrients listed above have specific anti-inflammatory roles in addition to their antioxidant, antiviral, immune-boosting, and pulmonary properties. However, what is at stake is the intake of these foods in combination. However, it is not recommended to receive them separately or supplements except for exceptions. For example, in countries or societies where the prevalence of vit D deficiency is high, or in young women during pregnancy requiring iron supplementation, or in the elderly who, due to physiological changes, require Zn or magnesium, for others, taking supplements seems to be unhelpful. Therefore, the general recommendation for supplements is only when a person has a particular micronutrient deficiency or is at risk for that micronutrient deficiency. However, recommending a diet that can have anti-inflammatory effects in addition to preventing, controlling, and treating RVI with an emphasis on immune-boosting, antioxidant, antiviral, and pulmonary function-enhancing effects is beneficial. Therefore, as indicated by the anti-inflammatory diet, foods and micronutrients with anti-inflammatory effects are recommended to be obtained through diet. On the other hand, it is advisable to limit/eliminate the intake of foods that have inflammatory effects.

Based on studies, significant components of an anti-inflammatory diet includes 1. turmeric, 2. ginger, 3. garlic, 3. onions, 4. saffron, 5. vit C sources such as citrus fruits, berries, and tomatoes, peppers, kiwi, papaya, caraway, mango, 6. vit D sources such as salmon, herring and sardine, enriched orange juice and milk, 7. food sources of Zn such as beef liver, lentils, oatmeal, herring, and poultry and 8. Omega-3 food sources such as walnuts, flaxseed, and marine sources such as shrimp and fish. In addition, according to an anti-inflammatory diet taking caffeine, vit A, selenium, magnesium, folates, B12, and B vitamins groups such as B6, B2, and B1 and fiber can lead to one's diet is anti-inflammatory.

On the opposite side, the dietary items that increase inflammation include saturated and trans fatty acids, mainly processed foods and meats, and hydrogenated oils. Therefore, they have no place in our anti-inflammatory diet, and it is recommended to limit their consumption. Salt intake also causes inflammation, which is recommended to reduce it to the lowest recommended level.

Studies that examined the association between the diets with various diseases showed that people on an anti-inflammatory diet are less likely to develop inflammatory diseases/conditions.

## 5. Conclusion

Given that the drugs used in the treatment of RVI also reduce the inflammation caused by the virus receiving anti-inflammatory diets and drug therapy would be helpful. Furthermore, the anti-inflammatory diet components have antioxidant properties, boosting the immune system, antiviral, and improving lung function, which can help at various RVI. Therefore, it can help get an anti-inflammatory diet and proper hygiene, such as regular hand washing, non-contact with suspicious individuals, distance observation, disinfection of surfaces, and following treatment protocols.

## Ethics approval and consent to participate

Arak University of Medical Science ethics committee approved Protocol and Methods (IR.ARAKMU.REC.1398.177).

## Consent for publication

Not applicable.

## Availability of data and materials

Data sharing does not apply to this article as no datasets were generated or analyzed during the current study.

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## Declaration of competing interest

The authors declare that they have no competing interests.

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