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COVID-19 and Nutrition Implications: A Review

Claudio Maioli[1], *Federico Cioni*[2], *Salvatore Ciappellano*[3]

[1]Department of Health Sciences, University of Milan Unit of Nuclear Medicine, ASST Santi Paolo e Carlo, Milan, Italy; [2]Clinical Nutrition Clinic, Val Parma Hospital, Langhirano, Parma, Italy; [3]Department of Food, Environmental and Nutritional Sciences, Human Nutrition Unit, University of Milan, Milan, Italy

Abstract. Coronavirus disease arose in 2019 (COVID-19) and has been defined a current global pandemic by the WHO (Word Health Organization). Several challenges have arisen on how to treat the disease and how to prevent it. A key role for prevention is to optimally support the immune system in the general population so that the immune response is as effective as possible. This depends also on an adequate nutritional intake able to strengthen the defenses against infection. In this review we will review the most important nutrients related to COVID disease defense.

Key words: COVID-19, nutrition, immune response, nutritional intake, defense

Introduction

The COVID-19 disease is increasingly widespread all over the world and starting from Wuhan (China) in December 2019 it spread rapidly around the world, generating a global pandemic (1-3). A healthy and functional immune system is essential to prevent and/or counteract infection, and this, among other factors, is also linked to an adequate and balanced diet (4,5). It is known that a nutritional status deficient in proteins can increase the risk of infection, related, for example, to low production of antibodies (6). It is also fundamental to have an optimal nutritional status to take under control the processes of inflammation and oxidative stress, all correlated with the immune system (7). The relationship between food compounds, nutrition, inflammation, and oxidative stress has been well analyzed and emphasized, for example, in the development of the anti-inflammatory dietary index (8). Nutritional components known to exert anti-inflammatory and antioxidant properties include omega-3 fatty acids (9), vitamin E, vitamin A (10), vitamin C (11), as well as a variety of phytochemicals, such as polyphenols (12) and carotenoids (13) which are widely found in plant-based foods. The fibers found in plant-based foods also have anti-inflammatory properties (14). Dietary fibers, and a variety of phytochemicals such as polyphenols, influence the intestinal microbiota (15), having prebiotic effects such as promoting the growth of bacteria associated with health benefits (for example Bifidobacterium spp.), and reducing potential pathogens such as Clostridium spp. These aspects are of interest for gastrointestinal complications reported during SARS-CoV-2 infection (16). Vitamin D has also been proposed as a nutrient that is able to interact with its own transcription factors (vitamin D receptor) or with the cellular receptor for viral entry, i.e., ACE2 (angiotensin 2 conversion enzyme), which inhibits the entrance of viral particles into the cell (17). Numerous mechanistic and clinical data show that vitamins, including vitamins A, B6, B12, C, D, E, Folate; trace elements, including zinc, iron, selenium, magnesium, copper and omega-3 fatty acids, in particular eicosapentaenoic acid and docosahexaenoic acid, play important and complementary roles in supporting the immune system (18). In this review, we highlight the importance of optimal nutritional status to strengthen the immune system during the COVID-19 crisis by focusing on the most relevant nutrients that contribute to the reduction of inflammation and oxidative stress.

Diet Nutrients that Strengthen the Immune System and Decrease the Risk of Infection.

Proteins

In situations where there is insufficient protein status due to low protein intake, i.e., below the recommended 0.8 and 0.9 g / kg body weight as respectively suggested by IOM (Institute of Medicine) and LARN (Reference levels of Energy and Nutrient intake) (19, 134), for example in individuals with economic difficulties in countries with low protein availability, there is an increased risk of infection (20). The poor pool of available proteins is also believed to result in a decreased amount of functionally active immunoglobulins and gut-associated lymphoid tissue (GALT), which together play a role in defending the intestinal mucosa against infection (21). Although the prevalence of protein energy malnutrition is low in Western countries, several sources of protein, particularly those derived from food products such as processed meats and cheeses, are high in calories and saturated fats and can aggravate post-prandial effects, promoting lipogenesis and increasing inflammation (22). In this regard, the pro-inflammatory aspects of proteins of animal origin and the anti-inflammatory properties of proteins of plant origin have been highlighted in a recent work (23). For example, diets that are rich in meat proteins increase colon monocytes (24), and it can be assumed that other components of the matrix such as saturated fats play a similar role as the absence of fiber does. The intake of high biological value proteins found in eggs, fish, lean meat (e.g. poultry) and whey proteins (or other fat-free milk proteins), when consumed with meals, can help to lower the lipogenesis and postprandial inflammation (25). The consumption of a certain amount of high biological value proteins is known to be the crucial component for an optimal production of antibodies (26). Branched-chain amino acids can maintain villous morphology and increase intestinal immunoglobulin levels, thereby improving the intestinal barrier and pathogen response (27). Some amino acids modulate the metabolism and functions of the immune system. For example, arginine supplementation increased T-cell response, and the number of T helper cells, rapidly returning to normal T-cell function after supplementation, compared to control subjects (28), suggesting a role in prolonged or repeated infection. Glutamine is required for the expression of a variety of immune system genes (29). Glutamine is an energy substrate for macrophages, neutrophils and lymphocytes, necessary for the identification of pathogens through the proliferation of immune cells and tissue repair (30). For example, in the immune system, glutamine plays a key role in controlling the proliferation of cells such as lymphocytes, neutrophils and macrophages (31). A protein-deficient nutritional status, characterized by low levels of albumin or prealbumin, but also low levels of iron and vitamin E related to poorer responses in influenza vaccination in the elderly, highlights the interaction between various nutrients and the immune response (32). In a study of 140 patients, diagnosed with COVID-19 IL-6 (interleukin 6), CRP (C reactive protein), and PCT (procalcitonin) levels were increased in 95 (67.9%), 91 (65.0%), and 8 (5.7%) patients, respectively, at admission. The proportion of patients with increased IL-6, CRP and PCT levels was significantly higher in the more severe disease group than in the more moderate disease group. Patients with IL-6> 32.1 pg / mL or CRP> 41.8 mg / L were more likely to have serious complications. These parameters can effectively assess disease severity and predict outcomes in COVID-19 patients (33).

Lipids

Fatty acids (FA) have been shown to affect homeostasis and the functioning of immune cells in mice, e.g., in epithelial, macrophage, dendritic, lymphoid, neutrophil and T and B cells (34). An increase in fibrinogen and high-sensitivity C-reactive protein (hs-CRP), a protein of the acute phase of hepatic inflammation, has been linked to consumption of saturated AGs, while lower levels of hs-CRP have been linked to polyunsaturated AGs (35). Omega-3 FA appears to have the most potent anti-inflammatory ability (36), although not all omega-3 FA have an anti-inflammatory effect. The intake of trans fatty acids, especially from foods that have been treated with drastic cooking techniques such as deep-fried foods, as potato chips, have been described as pro-inflammatory, being associated with increased levels of TNF, IL-6 and hs-CRP (37). The two essential classes of AGs, omega-6 and omega-3, are introduced with the diet as the human body is unable to produce them. The intake of omega-3 FA from fish and seafood has been shown to trigger anti-inflammatory reactions via oxygenated metabolites including resolvins and protectins (38, 39). Omega-3 FA include alpha-linolenic acid found in various plant sources (chia seeds, soybeans, avocados, etc.), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) mainly from seafood, such as salmon, mackerel, and tuna. Omega-6 FA, such as arachidonic acid, are mainly pro-inflammatory (40,41), as they are precursors of several pro-inflammatory mediators including eicosanoids (such as prostaglandins and leukotrienes derived from cyclooxygenase (COX) and lipoxygenase (LOX) enzymes, respectively (42). An imbalance of FA, such as saturated FA / unsaturated FA and omega-6 FA / omega-3 FA has an important negative implication for the homeostasis of the immune system, promoting the risk of onset of allergic diseases, autoimmune and altered conditions (43). In a study in mice, omega-3-derived mediator protectin D1 reduced viral replication, improved survival, and reduced symptoms after flu infection (44). The role of intake of lipids was discussed in viral infection. In mice, diets rich in lipids appear to play a crucial role both with respiratory and extra-respiratory complications due to virus infection, influenza A, linked to an increase in the viral load in the lungs and heart. This deficient antiviral response has been associated with signaling defects in the inflammatory response in mice, leading to elevated inflammation and damage to the lungs, as well as increased inflammation and heart damage, i.e., increased thickness and left ventricular mass (45). A high dietary fat content in mice was also associated with a reduction in the efficacy of the influenza vaccine through a reduced antibody response, due to macrophage dysfunction in the lipophilic environment (46).

Carbohydrates

Hyperglycemia induced by a high glycemic index and the respective high insulin response, due to a high consumption of easily assimilated carbohydrates (white flour, refined sugar), leads to an overload of the mitochondrial capacity and an increase in the production of free radicals (47). Even a single meal with a high glycemic load was associated with an immediate increase in inflammatory cytokines and CRP (48). Conversely, less processed, and low-glycemic foods, such as vegetables, fruits, nuts, seeds, and whole grains, do not cause inflammatory postprandial adverse effects (49). Interestingly, the use of a ketogenic diet, i.e., a diet high in fat but low in carbohydrates (<10% energy), appears to protect mice from the severity of influenza A virus infection in terms of morbidity and mortality through expansion of the delta gamma T cells in the lungs. These cells play an essential role in host defense against the influenza A virus (50).

Fibers

Dietary fibers are mostly made up of complex non-digestible carbohydrates. A significant reduction in hs-CRP concentration was observed with a fiber consumption of approximately 30 g / day (51). An advantage of taking whole grains is that it significantly contributes to a more balanced gut microbiota, which, in turn, can lower systemic inflammation: even small increases of just 5g of additional fiber per day can prove beneficial to improve well-being (52). A higher intake of whole grains has been associated with a decrease in hs-CRP, IL-6 and TNF-alpha, an increase in short-chain fatty acids (53), and a marked reduction in the risk of inflammation-mediated disease (54), such as CVD, T2D, cancer and obesity. The responses of macrophages to respiratory viruses are linked to the presence of distinct gut microbes. The importance of the gut microbiota for immune functioning has been demonstrated in animal models. Antibiotic treatment of the animals resulted in ineffective responses of macrophages to IFNs (interferons), with consequent negative effects in the control of viral replication (55). Furthermore, studies employing mouse models indicated that the microbiota helped establish a defense system against pathogens, such as blocking cell internalization (56), binding and destabilizing virion morphology, inhibiting further influenza virus infections (57), also suppressing other viral replications, such as the herpes simplex virus (HSV) -2 (58). The gut microbiota forms a dynamic environment that can be disturbed by virus infection but can be positively modulated by nutrients and non-nutrients present in food. COVID-19 has been associated with the development of damage affecting the respiratory system and the gastrointestinal system manifesting gastrointestinal symptoms such as nausea, vomiting, diarrhea, etc. (59). Damage to the digestive system can, in turn, affect the diversity of the gut microbiota and increase the risk of secondary bacterial infections.

Vitamin A

Vitamin A deficiency has traditionally been associated with an increased risk of infection. In fact, it is among the most abundant micronutrient deficiencies in the world, especially in countries with a low protein intake, especially animal-based proteins (60). However, vitamin A can also be obtained by the body when present in foods as a pro-vitamin A carotenoid such as beta carotene is the main source of vitamin A in individuals who eat few foods of animal origin (61). Vitamin A is important for the epithelium morphology, playing a role in its keratinization, stratification, differentiation, and functional maturation (62), which constitute a line of defense against pathogens. Vitamin A is involved in the formation of healthy mucus layers, such as those in the respiratory tract and intestines, which are necessary for the secretion of mucin. Retinol and retinoic acid are the active forms of vitamin A. Retinoic acids (all-trans and 9-cis) play a crucial role in regulating differentiation, maturation, and function of the immune system and in cells, for example in macrophages (63) and neutrophils (64). Retinoic acid promotes an immediate response to the invasion of pathogens through phagocytosis and the activation of natural killer (NK) T cells, which affect immunoregulatory functions, through cytotoxic activity (65).

Vitamin D

Intake of Vitamin D can derive from the diet when fish, eggs, fortified milk, and mushrooms are consumed. It can also be synthesized subcutaneously in the presence of UV rays using cholesterol as a source. The active form of vitamin D, calcitriol (1.25 dihydroxyvitamin D), formed because of hydroxylation by the liver and then by the kidneys, is the most important for its regulatory role in calcium homeostasis and therefore the health of bones, but it has also been shown to regulate the immune system (66). Indeed, the functioning of T cells is closely related to vitamin D (67). The function of vitamin D is still controversial due to its role in the prevention and therapy of influenza (68). Concerning human studies, contradictory data have been reported. A study conducted in China, performed on children who had received low and high doses of vitamin D, reported vitamin D administration protective effects against the incidence and severity of influenza (69). However, the fact that the study was based on individuals with Vitamin D deficient nutritional status might have played an important role in the outcomes. Vitamin D therapy, in a meta-analysis, improved conditions in individuals with chronic pulmonary obstruction (COPD), although it was not caused by infection alone (70), similar results were reported in another meta-analysis (68). Another review reported a reduced risk of influenza and COVID-19 infections and mortality (71), mainly due to the reduction of inflammatory cytokines and the increase in anti-inflammatory cytokines and antimicrobial peptides such as cathelicidin and defensins, and by modulating immunity, adaptive, such as reducing the response of T1 helper cells. Interestingly, vitamin D supplementation promotes the binding of the cellular entry receptor SARS-CoV-2 ACE2 (angiotensin 2 converting enzyme) to AGTR1 (angiotensin II type 1 receptor), reducing the number of viral particles that could connect to ACE2 and enter cell (72). A recent retrospective study including 780 confirmed SARS-CoV-2 infected patients determining mortality and associated factors, with particular attention to vitamin D status. Male and elderly patients with pre-existing conditions and lower than normal vitamin D levels were strongly associated with the increased probability of death, those with insufficient vitamin D status were nearly 13 times more likely to succumb (73). In Europe, COVID-related mortality appears attenuated with increasing latitude. For example, Nordic countries such as Finland and Norway that have mandatory vitamin D fortification or higher vitamin D intakes have some of the highest vitamin D levels in Europe but also lower mortality. Conversely, despite high sun exposure, older populations in Italy and Spain show a marked decrease in vitamin D nutritional status and higher COVID mortality rates (74). In a study of 50 hospitalized patients with COVID-19 it was found that 76% of patients were vitamin D deficient and 42% were selenium deficient. These findings suggest that a vitamin D or selenium deficiency can decrease immune defenses against COVID-19 and cause progression to severe disease (75). In a recent work, people at risk of influenza and / or COVID-19 are recommended to consider taking 10,000 IU / day of vitamin D3 for a few weeks to rapidly increase 25 (OH) D concentrations, followed by from 5000 IU / d. The goal should be to increase the 25 (OH) D concentrations beyond 40-60 ng / mL (100-150 nmol / L). For the treatment of people infected with COVID-19, higher doses of vitamin D3 may be useful (76).

Vitamin E

Vitamin E exists in the major forms of tocopherols and tocotrienols, with most of the research focused on the effects of the former. Tocopherols are present in high quantities in nuts and vegetable oils while tocotrienols are found predominantly in some seeds and cereals. Although vitamin E deficiencies are rare in humans, secondary deficiencies may occur, for example, as a result of an intestinal malabsorption disorder. It should be noted that to express its antioxidant effects, vitamin E works synergistically together with vitamin C, thanks to which its tocopheroxyl radical is reduced by vitamin C in the active form of tocopherol (77). Vitamin E has also been shown to regulate the maturation and functions of dendritic cells (78), which are important for regulating the immune system and directing the immune response (79). In addition to increasing the activity of NK cells, by modulating the levels of NO (80), the administration of vitamin E strengthens the humoral (B-cell) and antibody responses, both in animals and humans (81). Vitamin E has been shown to improve the formation of immune synapses of T lymphocytes and initiate activation signals of T lymphocytes (82). In a study of 2,216 smokers who received 50 mg / day of vitamin E for 5-8 years, supplementation with vitamin E was shown to reduce the incidence of pneumonia by 69% in elderly men (83).

Vitamin C

Vitamin C (ascorbic acid) is a classic antioxidant, able to directly neutralize free radicals' action. An increase in dietary intake of ascorbic acid was correlated with lower concentrations of C-reactive protein and plasminogen activator (84). Vitamin C also acts as a cofactor for several biosynthetic processes and the production of gene-regulated enzymes, monooxygenases, and dioxygenases, suggesting its immunomodulating effects (85). Ascorbic acid plays a role in the differentiation and maturation of T (86) lymphocytes. Vitamin C deficient status has been considered as an adjuvant measure in individuals with the common cold as well as pneumonia and positive effects have been found in some studies such as shortening the duration of the cold (87). In a double-blind controlled study with elderly participants, 200 mg / day of ascorbic acid for 4 weeks improved their respiratory conditions (88). In a meta-analysis of 3,135 children, supplementing 0.5-2 g / day of vitamin C did not prevent upper respiratory tract infections but reduced the duration of infection by 1.6 days (89).

Group B Vitamins

B vitamins are involved in many enzymatic processes. Individual studies have also shown that cobalamin (vitamin B12) can act as an immune modulator. For example, patients with vitamin B12 deficiency showed decreased CD8 + cells, a higher-than-normal CD4 / CD8 ratio, and decreased NK cell activity (90). The intake of vitamin B3, vitamin B6 and vitamin B12 in the form of niacin, pyridoxine, and cobalamin, respectively, were significantly associated with lower inflammation levels such as a decrease in CRP (91).

Minerals

Iron

Iron deficiency is widespread worldwide and its association with infectious diseases is well known (92). Vitamin A appears to modulate hematopoiesis and iron metabolism, improving the immune response to infectious diseases (93). Iron helps fight infections by allowing the proliferation and maturation of immune cells of T lymphocytes, as well as regulating the production of anti-bacterial cytokines, for example, by the action of neutrophils (94). The role of iron in bacterial and viral infections (95) has been critically reviewed, highlighting that homeostasis and iron levels are strictly controlled. During prolonged periods of iron deficiency, antibody production is typically reduced, as shown in experimental studies with mice exposed to the influenza virus (96). Immunosuppression has also been found in the elderly, correlating iron deficiency with cell-mediated immunity (97). In a study conducted on 485 hospitalized children aged 2-5 who received iron supplementation for 3 months, relapses of acute respiratory tract infections, urinary tract infections and gastroenteritis were significantly reduced (98).

Copper

Copper has been shown to play a role in the immune response to bacterial infections (99) and has been associated with the production and response of IL-2. High concentrations of copper can be found in leukocytes for invasion by microbes and appears to be employed by macrophages as a defense strategy (100), copper could play a role in secondary infections following viral infection. Copper is further involved in the proliferation of T cells and the production of antibodies and cellular immunity (101). A normal nutritional status of copper has been related to a more efficient defense against several bacterial infections, including E. coli, Salmonella, and tuberculosis (102). However, as the copper requirement is very low (it is often considered a trace element) and is ubiquitously distributed, copper deficiency is quite rare.

Zinc

Zinc deficiency is a major public health problem around the world (103) and also appears to be so in Western countries (104). A zinc deficient nutritional status has been associated with an increased risk of virosis and infections (105). The free non-chelated form of zinc has been shown to have direct antiviral effects in vitro, such as on rhinovirus replication (106). Zinc is an important cofactor for over 750 transcripts and therefore is involved in the synthesis of DNA and RNA (107), which are also necessary for the production of immune proteins. By stabilizing the tertiary structure or as an essential component of the catalytic site of enzymes (108), zinc acts as a cofactor for over 200 enzymes involved in antioxidant defense, in particular, anti-inflammatory SOD and SMAD proteins (109). In a recent review, the role of insufficient zinc level in the elderly and its relationship with pneumonia was highlighted (110). Mortality due to pneumonia has been reported to be twice as high in individuals with insufficient zinc nutritional status as in individuals with normal zinc levels (106). In a randomized, double-blind, placebo-controlled study, patients (n = 100) with common cold symptoms took 13.3 mg more zinc when symptoms were present (111). The results showed that, compared to placebo, zinc significantly reduced the duration of symptoms of the common cold, from 7.6 to 4.4 days.

Selenium

The role of selenium as an adjuvant therapy in viral and bacterial infections, and its relationship with influenza, hepatitis C and coxsackie viruses (112) has been reported. Selenium deficient nutritional status has been reported in multiple geographic regions including parts of China and several Western countries (113). Selenium plays an important role in metabolism because it is present in the form of selenocysteine in selenoproteins, some of which with antioxidant activity such as glutathione peroxidase (GPx1, GPx2, GPx3, Gpx4), thioredoxin reductase, iodiothyronine deiodinase while selenoprotein P seems to play the role Plasma transport of Selenium (114). Therefore, one of the primary roles of selenium is its ability as an antioxidant to counteract the action of ROS in the circulation, tissues and cell membranes (115). Selenium has been reported to be protective against heart damage due to cytomegalovirus and is involved in the proliferation of T lymphocytes and the humoral system, particularly in the production of immunoglobulins (116). In a prospective study of 83 patients with respiratory diseases requiring intensive care treatment, serum selenium levels at admission were 28% lower in the intensive care unit (ICU) group compared to a target group. Poor nutritional status of serum selenium was associated with a decrease in lymphocyte number and albumin concentration, a marker of protein nutritional status and correlated with increased CRP (117).

Polyphenols

Individuals who regularly consume fruits and vegetables have lower rates of inflammatory markers such as CRP, IL-6, and adhesion factors (118). This has been attributed to the high fiber content and higher concentrations of vitamins, minerals, and phenolic compounds in these foods, along with a lower calorie density. The significant presence of fruit and vegetables in the diet has significantly reduced serum inflammatory markers (119), improving microvascular reactivity and reducing CRP values (120), improving lipid profiles (121) and enhancing endothelial function (122). The role of polyphenols against influenza viruses, both in terms of prevention and treatment, has recently been revised. The main mechanisms highlighted were the suppression of neuramidase and hemagglutinin activity, which influence viral replication, viral hemagglutination, adhesion and penetration into the host cell, as well as the modification of cell signaling pathways (123). Within various cell models, the positive effect of coumarin, present in the leaves and seeds of herbaceous plants, has been demonstrated against viral infections such as HIV, influenza, enterovirus 71 (EV71) and coxsackie virus A16 (CVA16) (124). Theaflavin derivatives (black tea polyphenols) had a strong inhibitory effect against influenza virus in vitro (125). Garlic (*Allium sativum L*) is a functional food known for its immunomodulatory, antimicrobial, anti-inflammatory, antimutagen, antitumor properties. Garlic can be a preventive measure against COVID-19 infection to strengthen the cells of the immune system and to suppress the production and secretion of proinflammatory cytokines, as well as the hormone leptin derived from adipose tissue having a proinflammatory nature (126). Quercetin is a well-known flavonoid whose antiviral properties have been studied It has been shown that the co-administration of vitamin C and quercetin exerts a synergistic antiviral action due to the superimposition of antiviral and immunomodulating properties and the ability of ascorbate to make quercetin bioavailable, increasing its efficacy. The use of vitamin C and quercetin for both prophylaxis in high-risk populations and for the treatment of COVID-19 patients in addition to promising pharmacological agents such as Remdesivir or plasma can make significant positive contributions (127).

Bioactive foods

Kefir

Kefir is a fermented milk drink similar to low-fat yogurt made from kefir grains (128). Kefir and its probiotic content can modulate the immune system to suppress virus infections (e.g., Zika, hepatitis C, influenza, rotavirus) (129). The antiviral mechanisms of kefir involve increased production of macrophages, phagocytosis, production of positive differentiation clusters CD4 +, CD8 +, IgG, IgA and B cell immunoglobulins, T cells, neutrophils, as well as cytokines (e.g., interleukin-2, IL-12, interferon gamma (130). Kefir can act as an anti-inflammatory agent by reducing the expression of IL-6, IL-1, TNF-αand interferon-α Thus, kefir could be a significant inhibitor of the “cytokine storm” which contributes to the control of COVID-19 (131).

Propolis

It is a resinous material produced by honeybees from plant exudates, has long been used in the herbalist tradition and is widely consumed as a health aid and immune system enhancer. The COVID-19 pandemic has renewed interest in propolis-based products around the world; fortunately, various mechanisms of SARS-CoV-2 infection are potential targets for propolis compounds. Entry of SARS-CoV-2 into host cells is characterized by the interaction of the viral spike protein with the cellular angiotensin converting enzyme 2 (ACE2) and the serine protease TMPRSS2. This mechanism involves the overexpression of PAK1, which is a kinase that mediates lung inflammation, fibrosis, and suppression of the immune system. The components of propolis have inhibitory effects on the ACE2, TMPRSS2 and PAK1 signaling pathways; this antiviral activity has been reported both *in vitro* and *in vivo* (132).

Garlic

it is one of the most effective natural antibiotics against a broad spectrum of viruses and bacteria. Organosulfide compounds (allicin and alliin) and flavonoids (quercetin) are responsible for the immunomodulatory effects of this healthful spice. The viral replication process is accelerated with the major structural protease of SARS-CoV-2. The formation of hydrogen bonds between this serine-type protease and the bioactive compounds of garlic in the regions of the active site inhibits the replication of COVID-19. The daily dietary intake of garlic and its derivatives as adjuvant therapy can improve the side effects and toxicity of the main therapeutic drugs with the possible reduction of the dose used (133).

Conclusion

The viral disease from COVID-19 has become a worldwide problem and it is evident from all the data reported in the literature that a good overall nutritional status may contribute to prevention and a good ability to deal with the disease. An optimal dietary approach provides above all a correct protein intake. Among carbohydrates, complex carbohydrates should be consumed, avoiding simples ones (sugars) which increase the inflammatory state. The FA must be taken following the recommended quantities, limiting saturated fatty acids. Fibers must also be taken in the right quantities. As regards the group of vitamins, vitamin D seems to have an important regulatory role in preventing and fighting viral diseases and it is suggested to evaluate the state of vitamin D in individual subjects, possibly with the aim of integrating it. Vitamin C should also be taken in the recommended quantities. Regarding the group of minerals, it is important to have a correct Zinc intake, as Zinc deficiency remains a worldwide problem. We also recommend the intake of polyphenols given their antioxidant and anti-inflammatory properties. Our immune system plays a fundamental role in being able to fight this epidemic, and it is necessary to maintain it in the best possible reactive state. Moreover, it is important to gain further insights on new regulatory mechanisms to enhance our immune response and allow the maintenance of the best possible conditions for our immune system. This applies not only when it comes to COVID-19, but to all viral diseases that might develop over time.

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Correspondence:
Dr Claudio Maioli
Department of Health Sciences, University of Milan Unit of Nuclear Medicine, ASST Santi Paolo e Carlo, Milan, Italy
Email: claudio.maioli@unimi.it