Applied Food Research 3 (2023) 100291

Contents lists available at ScienceDirect

Applied Food Research

journal homepage: www.elsevier.com/locate/afres

# A systematic review on immunity functionalities and nutritional food recommendations to develop immunity against viral infection

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ARTICLE INFO

*Keywords:*
Unhealthy lifestyle
Immunity maintenance
COVID-19
Systemic inflammation
Healthy foods

ABSTRACT

Immunity plays a fundamental role in the maintenance and protection of the human body from infectious and pathogenic microorganisms. It requires regular intake of nutrients for proper functioning of the immune system. Due to an unbalanced lifestyle and consumption of ready-to-eat foods, immunity is being affected negatively. Inflammation and immunity are influenced by diet and nutrition. Simple sugars, trans fats, refined carbs, and processed meat, among other meals, may induce inflammation while simultaneously counteracting the anti-inflammatory benefits of omega-3 fatty acids. As a result, unhealthy food intake may enhance systemic inflammation in individuals, boosting the generation of IL-6. Dietary nutrition is a well-known aspect of immune system maintenance, with the significance of micronutrients prominently featured in a variety of scientific literary works. Currently, global population is susceptible viral infection such as COVID-19. This viral strain is directly attacking the immunity of the individual and bringing it at risk. When a patient's immune system isn't operating correctly, COVID-19 is thought to raise the harshness of the infection or make it more vulnerable to contagious diseases. This review paper will help in understanding the immune responses mechanism along with diet balance and maintaining the sufficiency of vitamins and minerals to fight against COVID-19 infection.

## 1. Introduction

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) superbug, a previously unknown virus, detected in December of 2019 and is the origin of the unprecedented contagious coronavirus sickness of the year 2019. COVID-19 was a worldwide epidemic in March, 2020 as proclaimed by World Health Organization (WHO) (Lange, 2021). Coronaviruses are enclosed and positive strained RNA viruses from the huge family that have the longest documented RNA sequences, up to 31 kb. Coronavirus cause a variety of diseases in primates (humans and animals) and avians (SARS-CoV). The SARS-COV-2 S-protein is comparable to the SARS-COV S-protein, but SARS-COV-2 has a 20-fold higher binding affinity for the (ACE-2) transmitter than that of the SARS S-protein (Ahmed et al., 2021). Direct contact with the infected individual's aerosol particles, accompanied by stroking the nose, eyes, and mouth, is the method of dissemination. Vertical transmission to newborns, also via faeces, appears to be a possibility (Mrityunjaya et al., 2020). Those infected with COVID-19, experience chronic respiratory disease. COVID-19 is much more dangerous and lethal in the pensioner and individuals with pre-existing medical and mental disorders than in the regular populace (Kim et al., 2020). Body parts that perhaps the SARS-CoV-2 attacks, according to what is documented thus far, have included the lungs, heart, renal system, and gastrointestinal tract. Tang et al. (2020) reported aberrant thrombosis in COVID-19 patients, which was linked to a damaged organ. The thymus is important for both lymphatic and endocrine functioning, and it is where T-cells originate, which are the lymphocytes responsible for adaptive immunity. In light of this, Rao et al. (2020) believes that the elevated mortality in COVID-

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https://doi.org/10.1016/j.afres.2023.100291
Received 10 October 2022; Received in revised form 6 February 2023; Accepted 17 March 2023
Available online 20 March 2023

19-affected older persons is predominantly owing to the body's immune deterioration caused by the downregulation of adaptive immunity. This supports our hypothesis that focusing on adaptive interferon (IFN – Type I interferons) gamma is a good idea. Foods can improve both innate and acquired defence, therefore the influence of nutrition on public health has traditionally been aimed of the studies (François et al., 2020).

Metabolic health is one of the most critical aspects that contribute to immune system performance. Because the immune system's actions are reduced due to a lack of vitality and critical nutrients, an individual who is food insecure is more susceptible to infections and disorders (Sharma, 2020). Nutrition and food are critical in maintaining lengthy health and preventing chronic conditions. Nutrition is vital for a healthy immune system, and both chronic starvation and excessive feeding can have negative effects on immune activation (Lange, 2021). Sharma (2020) accounted for certain vitamins (Vitamin A and C) along with essential amino acids, fatty acids, Iron, Copper, Zinc, and Selenium are all important nutrients for the immune system to be effective. In a patient with quasi-COVID-19, the migration of numerous immune cells, consisting of antibody-secreting cells along with follicular T cells, also engaged immunoglobulin IgG and IgM COVID-19-binding antibodies, has been documented (Thevarajan et al.,2020).

Elevated concentrations of pro-inflammatory cytokines and chemokines, such as granulocyte bacterial colonies stimulating factor, interleukin (IL)-2, IL-6, interferon (IFN)-induced protein vascular endothelial growth factor, monocyte chemoattractant protein-1, macrophage inflammatory protein-1, and tumor necrosis factor (TNF)-, along with lymphopenia, were found in the serum of some sick people during the initial phase infection with COVID-19 (Huang et al., 2020; Wang et al., 2020). Whereas, increase in anti-inflammatories like IL-10, IL-1RA, and IL-4 which are T-helper 2 (Th2) cytokines were also noted (Huang et al., 2020; Wang et al., 2020). The preliminary data imply that COVID-19 may be recognized by the immune system and mount a serious immunological response throughout many cell types, resulting in good infection healing in circumstances of mild to moderate symptoms (Gorji et al., 2021). This builds up summarised current findings on the evolution of human immunity as well as anthologizes list of studies that show that supplementing with the aforementioned nutrients can aid in the fight against COVID-19 in particular.

## 2. Mechanism of immune system in humans

The immune system has originated to shelter the host from the vastness of space of hazardous microbes that are always fluctuating. Immunity also aids the recipient in the removal of inadvertently ingested harmful substances and allergens that enter through mucosal surfaces. The ability of the immune system to tell the difference between self and non-self is critical for creating a defence against an invading allergy, toxin, or virus. The host uses both adaptive and innate systems to recognize and eliminate pathogenic microorganisms, both of which need self-non-self-bigotry (Chaplin et al., 2010).

### 2.1. Types of immunities

#### 2.1.1. Innate immunity

The first line of protection is innate immunity against infection. The overall majority of innate immunity elements are relevant before contamination and comprise a collection of virus-tolerant procedures which are not particular for a single pathogenic but also contain biological as well as molecular elements that recognize subclasses of chemicals unique to commonly occurring illnesses. Innate immunity relies on phagocytic cells like macrophages and neutrophils, as well as barriers like skin and a variety of germicidal chemicals produced by the host. Kanneganti et al. (2020) stated that innate immunity is the initial line of protection against infections which includes SARS-CoV-2. Innate immune mechanisms help recognize and eliminate infected cells, integrate, and hasten the generation of adaptive immunity, and restrict viral penetration, replication, translation, and assembly. Pattern recognition receptors (PRRs) on cytosols, endosomes, and cell surfaces respond to Pathogen-associated molecular patterns (PAMPs) by activating inflammatory responses and programmed cell death. On another side, excessive immune stimulation can lead to systemic inflammation and catastrophic disease (Diamond & Kanneganti, 2022).

#### 2.1.2. Adaptive immunity

As opposed to the innate immune system's wide responsiveness, which would be shared by all members of a species, adaptive immunity somehow doesn't kick in until the individual is confronted with a pathogenic threat. The adaptive defence is significantly more refined, allowing for particular identification of foreign particles as well as the selective proliferation of cells equipped to specifically target diseases and the expansion of immunological memory. Dendritic cells (DCs) assess for external antigens, bridging the responses of adaptive and innate immunity. T and B lymphocytes are important component cells for adaptive immunity (Gray & Gibbs, 2022). Adaptive immunity has a high degree of specificity when responding to a stimulus, as well as the extraordinary trait of "memory." A compatible immune response to an antigenic determinant typically develops between five and six days after antigen treatment. A memory reaction is triggered by prolonged exposure to the very same protein at a later time: the immune response to the second challenge is faster, bigger, and much more successful in neutralizing and eliminating the infection than the first. White blood cells, as well as the antibodies and other chemicals they create, are the primary agents of host defence. According to Chowdhury et al. (2020) white blood cells flow throughout the body via blood vessels and are a functional part of the immune system. By transporting cells and fluids between blood and lymphatic channels, the lymphatic system keeps an eye out for invasive bacteria. Antigens can be present in many niches inside each lymph node. Immune cells and other particles can enter lymph nodes through lymphatic veins. As they enter the bloodstream, they are disseminated to tissues over the whole body. They maintain this processing by probing the lymphatic system for external antigens followed by gradually re-entering it. In lymph nodes and the spleen's partitions, immune cells congregate, function, and contribute to the battle against invaders.

### 2.2. Immune system reacting towards viral infection

Innate and adaptive immunity are two types of immunity in our bodies that work together to prevent pathogens from invading our bodies. The primary components of the innate immune system include physical and epithelial barriers, dendritic cells, phagocytes, and natural killer cells. Notably, natural killer (NK) cells are considered as one of the most essential components of the innate immunity, with effector functions that do not require any prior activation (Jeyaraman et al., 2021). As, per the investigation done by Reusch et al. (2021) neutrophils are an important part of the cell's first line of defence against pathogens. They phagocytose microorganisms and clean them by fusing proteolytic enzymes, defensins, antimicrobial peptides, or reactive oxygen species (ROS) with their cytoplasmic granules. They can also generate neutrophil extracellular traps (NETs), which seem to be continuous releases of sections of the nucleus and granules. The progressive down regulation of neutrophils in circulation causes them to lose their ability to form NETs.

### 2.3. Virus - induced specificity of natural killer cells

Natural killer (NK) cells fall in the category of lymphocytes that help the immune system respond to infections initially. NK cells came in existence because of their potential to lyse tumour cells *in vitro*. They are now known to regulate a variety of immunological processes, including virus defence and immunological homeostasis. NK cells fulfil these roles by secreting chemokine and cytokines, which they use to interact with neighbouring cells. NK cells are innate immune cells that don't have altered antigen receptors and instead of that, it monitor their surroundings through pro-inflammatory cytokine receptors and germ line-encoded stimulating proteins for hazard or pathogen signals. Certain fractions of the NK cell compartment express a group of such triggering receptors at arbitrary. These receptors help to the particular stimulation and population expansion of defined NK cell subsets, which then replicate some properties of adaptable cells, after interaction of the corresponding viral ligand (Hammer et al., 2018). Hammer et al. (2018) mounted that NK cells use a panel of germ line-encoded receptors with both the activities (Activation and Inhibition) to sense their surroundings. NK cells are innate immune cells that don't have altered antigen receptors and instead monitor their surroundings through pro-inflammatory cytokine receptors and germ line-encoded stimulating proteins for hazard or pathogen signals. The aggregate of signals received from the specific receptors is what triggers the functional activities of certain NK cell. Inhibitory receptors, like KIRs (killer cell immunoglobulin-like receptors') in humans and Ly49 family receptors in mice are an important part of the NK cell receptor array. These inhibitory receptors bind to MHC class I and so keep NK cells from attacking normal host cells. Moreover, because of the down-regulation of MHC class I proteins that often occur during tumour formation and viral infection, NK cells can recognize changed host cells by attaching self-molecules to inhibitory receptors and recognizing missing oneself.

## 3. Immune response methodology of host amid COVID-19 infection

Considering the current disease outbreak solely from a scientific standpoint, and implying that the bulk of humanity has no elongated bridge to other members of the coronavirus community (Braun et al., 2020), the initiation of SARS-CoV-2 into the global species is one of the most significant evolutionary events in the last century (Morens et al., 2020). In such an adaptive environment, Vabret et al. (2020), Mantovani & Netea (2020), and Amor et al. (2020) proposed that a fairly exclusive role should be given to the innate immune system. The cell-autonomous action of virus particles, which would be affected by the biology of viral entryway sensors and co-receptors and the cellular processes that control the length of a virus's life span, is an essential part of innate immunity (Cyranoski, 2020; Hoffmann et al., 2020; Wu et al., 2020; Yao et al., 2020). In agreement with Callaway (2020) and Korber et al. (2020), the virus confronts the current beings as a hive of genetic variants in the SARS-CoV-2 outbreak. Virus replication processes and infection may still be vulnerable to significant genetic alterations, allowing some virus strains to gain an evolutionary edge. These types of functioning are in full motion, and, they are speeding up as more people become afflicted. Infected patients need to be monitored for alterations at starting stages of the antibody action to the virus, which are primarily driven through contagious cells and starting contacts with nearby innate immune cells. When studying essential host defensive mechanisms, all the parameters which are critical for such a starting encounter of a novel virus with a variety should be evaluated.

According to the Berlin et al. (2020) and Gandhi et al. (2020), because the bulk of the phases in the virus-host relationship will follow a typical distribution of qualities or factors necessary to decide the interaction's conclusion, it's not surprising that therapeutically reported disease regimens vary greatly. For illustration, a contaminated cell's stimulation of an antiviral reaction may receive the same treatment in the community, with moderate, middle, and strong respondents, resulting in varying intensities of cellular responses and, as a result, very diverse downstream effects such as in the innate immune system. Fig. 1 depicts significant host defence frameworks that may be especially susceptible to diverse consequences in the world population, due to both genetics and environmental factors, and in our efforts to analyse the functions of the innate immune system in infectiousness, viral propagation, and the course of sickness, as well as long-term conclusions, this should be a significant focus. Schultze and Aschenbrenner (2021) believe that conceptualizing the relation of innate immunity and the virus in this way, they will be able to focus on the key phrases first, which will allow us to focus on important steps afterward to be confirmed in further research.

### 3.1. The interaction of COVID-19 with neutrophills

Soy et al. (2020), Sokolowska et al. (2020) reported that moderate COVID-19 individuals had increased levels of cytokines [such as IL-1, IL-6, IL-17, TNF-] and pro-inflammatory chemokines such as CXC-chemokine ligand (CXCL) 1, CXCL2, CXCL8, CXCL10, CC-chemokine ligand (CCL) 2, CCL7, and neutrophil colony stimulation factor (G-CSF). The effects of these regulators on neutrophil maturation, activation, and recruitment have been frequently covered (Fig. 2). G-CSF interacts with the receptor on neutrophil precursor cells, which causes multiplication and the production of neutrophils from the bone marrow, according to research (Liew et al., 2019). IL-17 produced by neutrophil-regulatory T cells influences G-CSF formation, while IL-23 secreted by macrophages and DC cells influences IL-17 concentrations (Cui et al., 2021).

### 3.2. Importance of neutrophils in viral infection

Though antiviral resistance has typically been seen to be a role of the adaptive immune system, there are indications that innate immunity plays an influencing role in the patient's reaction to viruses. Polymorph nuclear neutrophils seem to be the most prevalent leukocytes in the bloodstream, accounting for 50–70% of the white blood cell count and contributing to the innate immune response versus invading microbes in the initial stages. Neutrophils are attracted to the area of inflammation within minutes of bacterial infection and serve a key role in defending the body from infections (Naumenko et al., 2018). Stegelmeier et al., (2019) conveyed that myeloid cells (neutrophils) have pattern recognition receptors (PRRs) that recognize pathogen-associated molecular patterns to recognize invading pathogens (PAMPs). PAMPs are nucleic acids that are identified by a subgroup of PRRs, or toll-like receptors, in the case of viruses (TLRs). TLR3, TLR7, and TLR8 detect RNA viruses, but TLR9 detects DNA viruses. When influenza viruses connect to endosomal TLR7 in neutrophils, their increased ingestion acts as an antiviral (Cui et al., 2021). TLR4 is involved in the human defence against influenza infection, even though influenza viruses are not connected to lipopolysaccharide (LPS) Stegelmeier et al. (2019). According to Cui et al. (2021) TLR4 deficiency, for instance, reduces neutrophil phagocytosis of apoptotic cells by increasing fatality in influenza virus-infected mice. However, after infection with viral pathogens such as human respiratory syncytial virus, human metapneumovirus (HMPV) Soto et al. (2018), rhinovirus, coronavirus, mouse adenovirus type I measles, and influenza A virus adenovirus mouse cytomegalovirus, neutrophils are found in the lungs of mice, rats. It's unclear whether neutrophil recruitment and activation benefit the host by assisting in host defence during viral infections where the pathogen multiplies intracellularly, or whether their presence is a downstream effect of local inflammation that contributes to tissue damage and sickness, according to Schönrich et al. (2016).

## 4. Nutritional insufficiency in SARS-CoV-2 infected patients

The connection between nutrition and the immune system is well established, that is why its role and importance in COVID-19 are being studied so closely (Butler & Barrientos, 2020). While there is no medication for COVID-19, consumption of nutritional food appears to boost the mechanism of the immune system, lowering the risk of infection and hastening fast recovery in those who are sick (Ruiz-Roso et al., 2020). This fact is especially notable in light of the pandemic's healthcare overload, emphasizing the functions of nutrition in overall health and immunity. The Mediterranean diet, as well as other nutritional regimens that minimize inflammation and chronic disease possibility, may lower COVID-19-related severe illness and mortality (Greene et al., 2021). Vitamins A, B (vitamins B6 and B12, folic acid), C, D, and the minerals Mg, Cu,

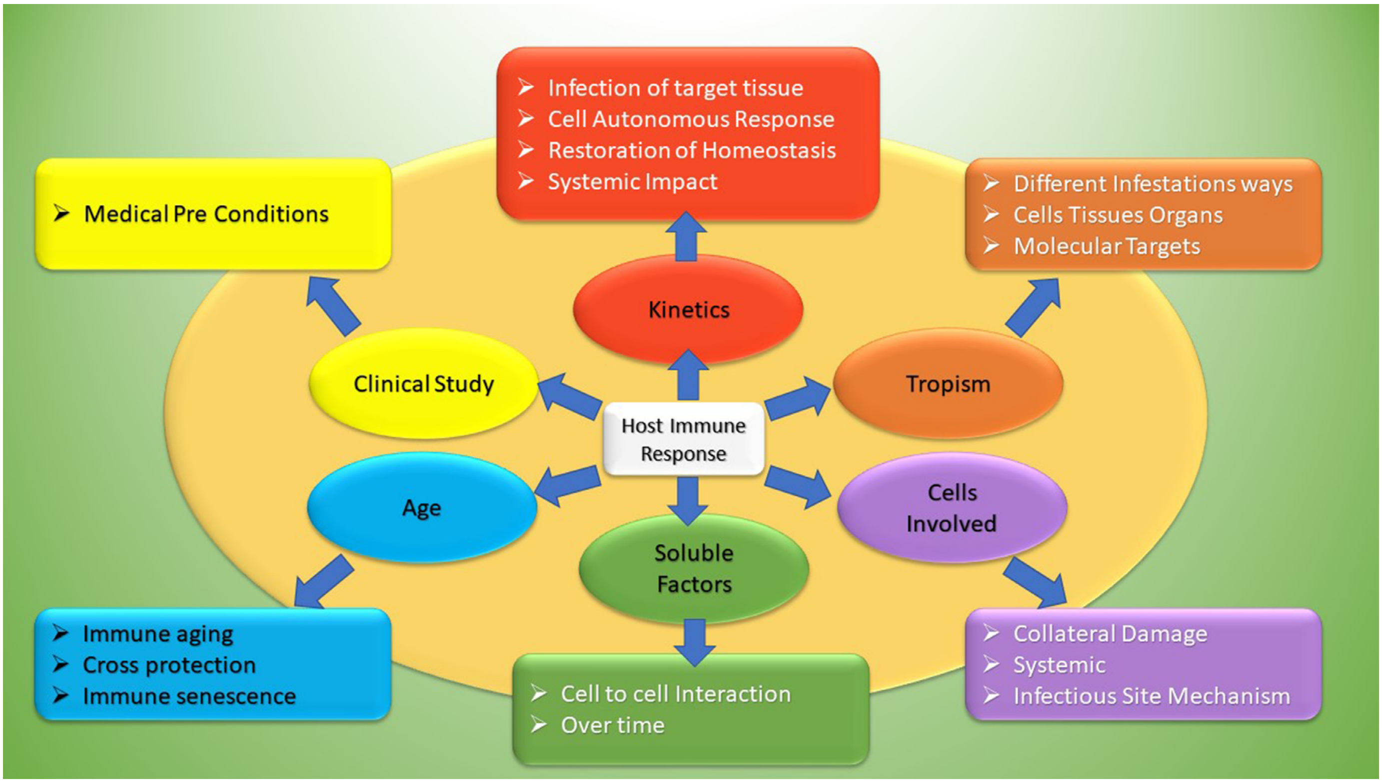


**Fig. 1.** Mechanism of the immune response during COVID-19 infection.

Zn, Fe, and Se are also required for optimized immunological responses (Richardson & Lovegrove, 2021). As a result, it's plausible to assume that COVID-19 propagation could be assisted by diminishing infection and reinfection resistance due to deficits in certain micronutrients, as well as poor nutritional conditions. Vitamin D is the most investigated micronutrient concerning COVID-19 as the vitamin D receptor is represented in almost every variety of immune cells (for example, T and B lymphocytes, monocytes, macrophages) (Sassi et al., 2018). So, the immune system's appropriate operation will be governed by the bio accessibility of vitamin D in the cells. As deficiency of vitamin D has not been found connected with a risk of COVID-19 infection, there is a connection between illness possibility and vitamin D (Pereira et al., 2022).

As a result, those with the most severe COVID-19 had a 64 % higher vitamin D insufficiency than those with the milder form. When vitamin D levels are low, COVID-19 increases the risk of hospitalization and fatality (Pereira et al., 2022). According to some evidence by Detopoulou et al. (2021), other micronutrients appear to affect the human immune system. However, short research has been done to link them to the likelihood and/or possibility of COVID-19 (Gasmi et al., 2020; Im et al., 2020). While most hospitalized patients do not have vitamin B1 or B12 deficiency or Zn deficiency, there is at least one nutrient deficiency in the vast majority (Im et al., 2020). Selenium deficiency, vitamin B6 deficiency, and folate deficiency were discovered in 42 % of COVID-19 infected patients (Im et al., 2020). These results suggest that selenium deficiency, when combined with a deficiency of vitamin D, may impair immune responses to COVID-19, resulting in disease development. Selenium is needed for the proliferation, differentiation, and processing of many innate immune system cells perfectly. As selenium helps with antibody production and development so, it also plays an important role for the adaptive response (Saeed et al., 2016).

However, further in-depth and large-scale research is needed to back up these conclusions. Vitamin C is another vitamin that affects respiratory tract infections; because of its antioxidant properties, this is one of the most common problems for COVID-19 infected patients (Patterson et al., 2021). Hundreds of genes are regulated by vitamin C in immune cells, which is a pleiotropic and essential activity in the immune system (Chen, 2020). Levels of serum vitamin C were found low in the maximum of COVID-19 patients who were critically ill. Furthermore, along with age vitamin C is observed to be an equally dependent endangered factor for COVID-19 infection (Arvinte et al., 2020). Although other micronutrients play a role in immunity, there is little evidence that their levels are linked to COVID-19 prevention and therapy. However, a study that looked at the relationship between population nutritional quality and COVID-19 epidemiological data in ten European nations found that poor iron and vitamin B12 consumption was linked to increased death counts from COVID-19 (Galmés et al., 2020). Low B12 levels cause an increase in homocysteine and methylmalonic acid, which eventually leads to, oxidative stress, inflammation, and reactive oxygen species production (Mikkelsen et al., 2017). Iron is engaged in several immune functions and is a required component of several enzymes involved in critical immune cell functions (Agoro et al., 2018).

Another factor to consider is the nutritional health of patients who were in the hospital for a long time, particularly those in intensive care (>5 days) (Haraj et al., 2021). Despite receiving a specialized diet that includes trace elements and vitamin C supplementation throughout their stay in the hospital, almost 50.0 % of COVID-19 patients with age independence remain malnourished (Abate et al., 2021).

As a result, over 40% of patients lose 5% of their body weight during their hospitalization, a condition known as cachexia (Anker et al., 2021). On a biological level, these patients also suffer hypoproteinaemia, hypoalbuminemia, anaemia, hypomagnesemia, hypocalcaemia, and vitamin D deficiency (Haraj et al., 2021). Immobility, which may play a significant role in COVID-19 muscular atrophy and sarcopenia, exacerbates this (Van Aerde et al., 2020). While there are no specific therapies for COVID-19 patients who have been admitted to the hospital, Nutritional support and rehabilitation should be the focus of treatment. Exercises wherever possible to reduce the long-term disability caused by acute COVID-19 disease (Anker et al., 2021). The link between COVID-19 and

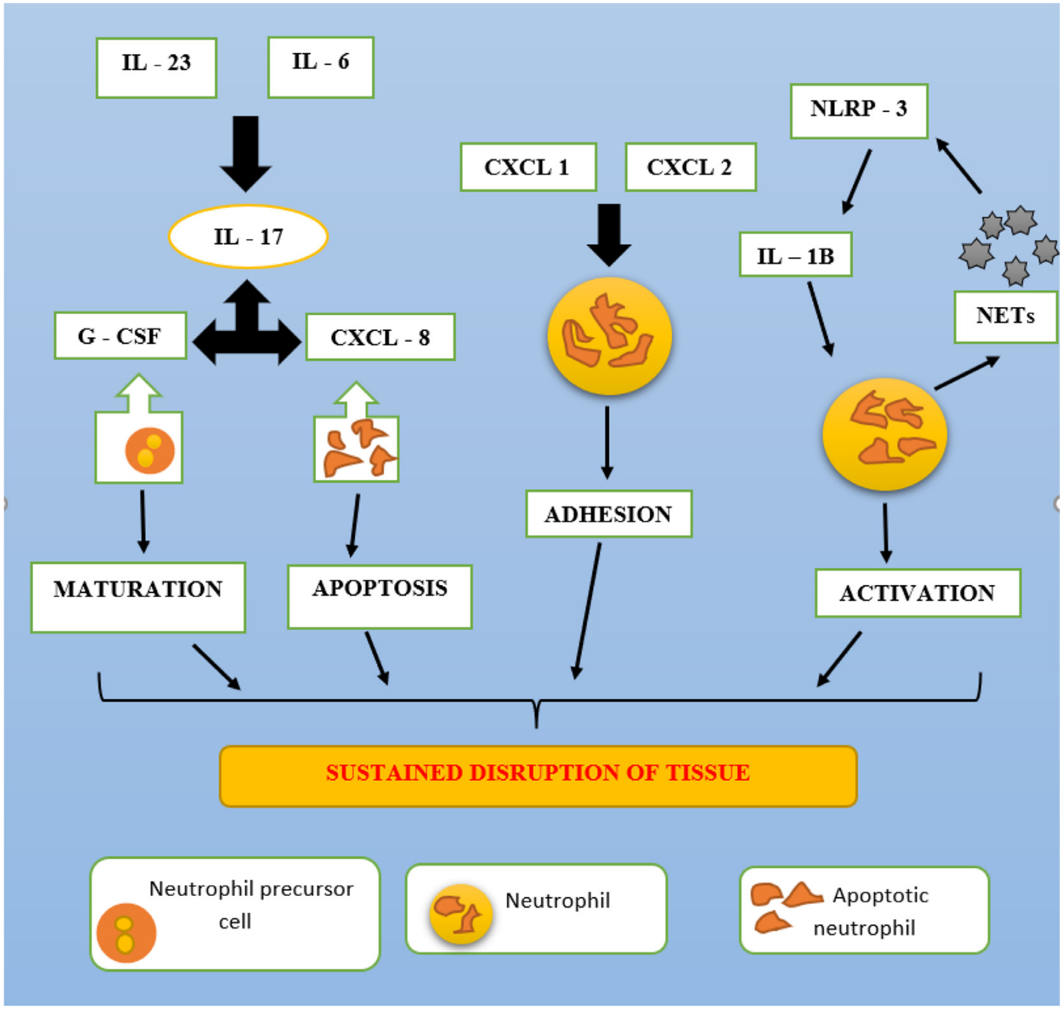


**Fig. 2.** Interaction process between cytokines and recruited neutrophils.

nutrition is becoming apparent every day. Although a deficiency in certain nutrients is not a determining factor in the spread of COVID-19, it is a predictor of the illness. Inadequate iron and vitamin B12 consumption, as well as vitamin C, D, and selenium deficiencies, have all been linked to an elevated risk of COVID-19-related hospitalization. The majority of patients who have spent more than five days in the hospital, have presented with malnutrition/cachexia after they leave, despite getting individualized nutrition during their stay. Health organizations are hereby encouraged to enhance nutritional planning and promotion for proper supplementation of food which is directly connected to COVID-19 infections, particularly in older age group (Gröber & Holick, 2021). COVID-19 survivors should also be monitored for 3 - 6 months with, clinical, laboratory tests, and anthropometric to ensure proper recovery (Yang et al., 2019).

## 5. Maintenance of immune system

Although dramatic changes in societal attitudes and socioeconomic norms had a detrimental effect, a well-balanced nutrition diet is still seen as a critical challenge in boosting immunity to battle a variety of ailments (Thirumdas et al., 2021). The research by Gombart et al. (2020), sparked a spike of curiosity about the relationships between nutritional status and immunological performance. Since then, numerous research reports have been disseminated detailing the probable beneficial activities of micronutrients in COVID-19 physiopathology.

Investigations by Wang et al. (2021) reveal that low levels of micronutrients such as vitamins C, D, Se, and Zn, are linked to a rapid increase in the risk of SARS-CoV infection and worsening illness levels. Citrus fruits, garlic, broccoli, and leafy greens all help with a weakened immune system. According to high-quality research, supplementation of vitamin C (therapeutic doses of 90 mg/day for men or 75 mg/day for women) can dramatically lessen the duration of a respiratory illness in adults and children (Mishra et al., 2020). Various nutritional groups with functional components are categorized in Table 1.

## 6. Foods and nutrients boosting immunity

For the healthy and proper functioning of immune cells, there is always a requirement for appropriate nutrients. For addition in the body's defences against microbial infections and inflammation, there are specific diet regulations. Many micronutrients are the necessities of the human body at every level of immunity. Some nutrients have been found as required for immune cell functioning and growth, consisting of vitamin C, D, Zn, Se, Fe, and protein. Numerous plant and animal diets include these components. Diets lacking in variety and nutrition, processed and minimally processed foods, can harm an immune system's health. A Western quality eating habit is high in refined white sugar, red tender meat, and also very less quantity of fruits and vegetables which leads to alteration of healthy microorganisms of the intestine, and results in inflammation in the gut and immunological suppression.

**Table 1**
List of nutritional groups with detailed components used in boosting human immunity.

| Nutritional groups for boosting immunity | Components | Functional Properties | Refs. |
|---|---|---|---|
| Amino acids | Glutamine | ➢ Amino acid synthesis, Gluconeogenesis, Formulation of glutathione and urea, increases ammonia excretion.<br>➢ Stimulates cell growth and serves as a key source of carbohydrate skeletons.<br>➢ Aids in the growth and stability of the intestinal mucosa, as well as improving the function of the intestine in affected patients. | Lobleyet al. (2001) |
| | Arginine | ➢ In healthy individuals, arginine administration raises blood lymphocyte, proliferation, and suppressor T-cell counts.<br>➢ In rats with tumor transplants, it increased the phagocytic activity of alveolar macrophages.<br>➢ Helps in DNA replication as well as in Cell Division.<br>➢ Nitric oxide's only precursor. | Geiger et al. (2016);<br>Ibrahim et al. (2016) |
| Vitamins | Vitamin A | ➢ Enhances Cell-mediated as well as Humoral immunity.<br>➢ Vitamin A and its metabolites influence aspects of innate immunity, such as neutrophil maturation control.<br>➢ It plays a role in physiological functioning, differentiation of epithelial tissue, and the maturation of immune cells.<br>➢ Its insufficiency causes changes in immunological response, extreme sensitivity to a variety of infections, and impaired intestinal barrier.<br>➢ Reduces deaths and mortality in infectious diseases such as diarrheal, measles, pneumonia-related measles, HIV/AIDS, and malaria. | Bendich, (1991)<br>Calder et al. (2020);<br>Norman et al. (2008) |
| | Vitamin B6 (pyridoxine) | ➢ Its deprivation affects lymphocyte maturity, development, as well as antibody production.<br>➢ Th1 production is ceased due to deficiency of vitamin B6.<br>➢ Interleukin-2 is affected by a lack of vitamin B6 (IL-2).<br>➢ Helps in Natural Healing.<br>➢ Protect against various viruses. | Ibrahim et al. (2016);<br>Calder et al. (2020);<br>Cheng et al. (2006);<br>Magginiet al. (2007) |
| | Biotin (Vitamin B8) | ➢ Act as coenzyme.<br>➢ Its deficiency harms the cellular and humoral immune systems and inhibits thymocyte development and decreases antibody manufacturing. | Crisp et al. (2004);<br>Báez-Saldañaet al., (2004) |
| | Vitamin B9 (Folic acid) | ➢ It is the predecessor of the coenzyme tetrahydrofolate.<br>➢ Engaged in the production of nucleic bases, purines, and pyrimidines.<br>➢ A lack of folic acid resulted in thymus and spleen shrinkage, as well as a reduction in the number of circulating T-lymphocytes. Low Folate levels have problems with neutrophil functionality. | Calder et al. (2020) |
| | Vitamin B12 (cobalamin) | ➢ Vitamin B12 is required for the production and maintenance of DNA.<br>➢ It is involved in glucose, protein metabolism, and lipid in addition to hemopoiesis, among other metabolic pathways. Hemoglobin levels drop as a result of cobalamin insufficiency.<br>➢ Mechanical hemolysis, Elevated lactic dehydrogenase levels, vasoconstriction, thrombocytopenia, intravascular coagulation thrombosis, low reticulocyte count, and renal pulmonary vasculopathy are all signs of cobalamin insufficiency.<br>➢ Macrocytosis, dizziness, peripheral neuropathy, ataxia, depression, schizophrenia, psychosis, cognitive problems, paralysis, fibromyalgia-like symptoms, muscle cramps, and weariness are all signs of vitamin B12 insufficiency. | Batista et al. (2022)<br>Tee et al. (2020)<br>Kulkarni et al. (2021) |
| | Vitamin C | ➢ Helps in the synthesis of Collagen.<br>➢ This vitamin shields the adaptive and innate immunity system from oxidative stress by supporting its cellular functioning.<br>➢ Its deficiency causes a reduction in microbial activity and motility of neutrophils, macrophages and vulnerability to microbial infections increases. | Hemila (2017);<br>Chandra (2004);<br>Chandra (2004) |
| | Vitamin D | ➢ Helps in calcium metabolism and bone<br>➢ Homeostasis in the human body.<br>➢ Play a vital role in both immunities.<br>➢ Enhances phagocytosis, and superoxide production.<br>➢ It encourages monocyte differentiation and Dendritic cells process antigen.<br>➢ It also plays a role in pulmonary resistance. Its insufficiency leads to a variety of respiratory illnesses, affecting both cytokine and immunoglobulin production.<br>➢ It reduces adipose tissue inflammation, improves epithelial combination, also stimulates the production of antimicrobial peptides. | Gombartet al. (2005)<br>de Tena et al. (2014)<br>Gao et al. (2013) |
| | Vitamin E | ➢ Serve as antioxidant<br>➢ Protect against oxidative damage to immune cells.<br>➢ Helps in enhancing immune function against any pathogen.<br>➢ Vitamin E has been investigated as a possible treatment for several human ailments, including heart disease and cancer. | Meydaniet al. (2005);<br>Meydaniet al. (2004)<br>Paeet al. (2012)<br>Chandra (2004) |

(*continued on next page*)

**Table 1** (*continued*)

| Nutritional groups for boosting immunity | Components | Functional Properties | Refs. |
|---|---|---|---|
| Minerals | Selenium (Se) | ➢ Selenium intake boosts the cellular immune response by increasing interferon (IF) and other cytokines, T-cell proliferation.<br>➢ Selenium deficiency has been associated with a decrease in the functioning of natural killer cells and an elevation in mycobacterial illness.<br>➢ In animal studies, selenium depletion impacts various aspects of innate and acquired immunity, including T and B-lymphocyte functionality, antibodies generation, and disease sensitivity. | Beck and Melinda (2001) |
| | Iron (Fe) | ➢ Iron deficiency causes thymus atrophy.<br>➢ By boosting the immune system, diets high in Fe can help people from contracting COVID-19. Iron deficiency reduces the proliferation of T-lymphocyte. | Calder et al. (2020)<br>Ahluwalia et al. (2004)<br>Malan et al. (2015) |
| | Magnesium (Mg) | ➢ Magnesium is required for cellular metabolism, which includes immune system cells.<br>➢ It is involved in the protein synthesis of resistance components; serum antibody levels could be used as a sensitive indicator of Mg deficiency or inadequate status. Mg2+ is a vital cofactor in cells, where it binds to DNA, RNA, the cellular energy carrier ATP, and enzymes.<br>➢ T-cell receptors (TCRs) at the surface of T-cells identify and respond to external antigens. | Son et al. (2007)<br>El-Mowafiet al. (1997)<br>Wu et al. (2011) |
| | Zinc (Zn) | ➢ Zinc deficiency has been linked to a drop in immunological progenitor cell counts, as well as a reduction in naive B-lymphocyte production and thymic shrinkage.<br>➢ Several components of innate immunity are also affected, including phagocytosis and natural killer cell activity.<br>➢ Zinc helps neutrophils generate extracellular traps that catch bacteria.<br>➢ Zinc suppresses RNA polymerase replication in RNA viruses like coronavirus. Zinc may be important in the host's fight against RNA viruses. | Kaushik et al. (2017)<br>Hasan et al. (2013) |

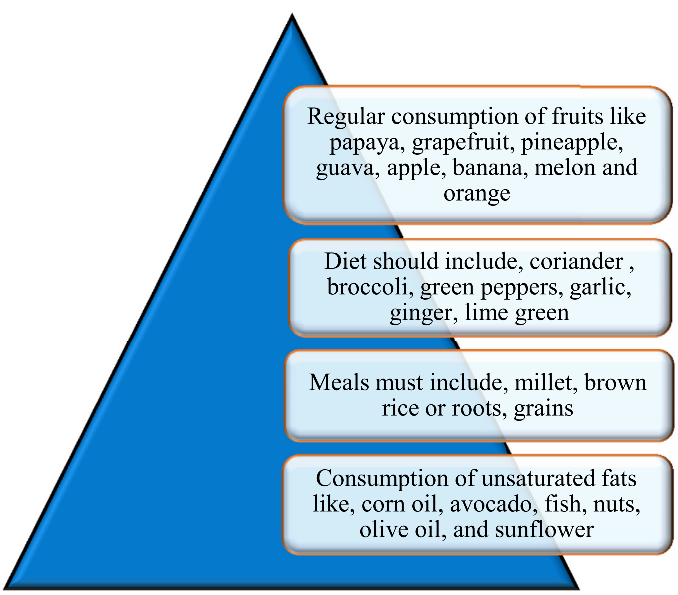


**Fig. 3.** Suggested food items to prevent lowering of immunity.

A schematic representation of a recommended diet to boost immunity during Covid infection is shown in Fig. 3 (Aman & Masood, 2020).

### 6.1. Significance of nutrients in enhancing the immunity of Covid-19 infected patients

#### 6.1.1. Vitamin A

Jayawardena et al. (2020) accounted that vitamin A has a key function in immune function enhancement and immune response modulation in both cells mediated immunity as well as in humoral immune actions. Its supplementation to babies has been found to boost immunoglobulin response to various vaccines, such as measles and anti-rabies immunizations 2.1 times (Jayawardena et al., 2020). In the respiratory system, vitamin A serves a special function in reducing harmful inflammation, promoting respiratory epithelium healing, and preventing fibrosis. Due to unique effects on lung and liver storage brought on by inflammation and reduced renal function, vitamin A insufficiency may arise during COVID-19, and supplements may be required to restore appropriate status. In order to improve the clearance of a primary infection and reduce the risk of secondary infections, vitamin A is crucial for sustaining innate and adaptive immunity .

#### 6.1.2. Vitamin C and E

Vitamins C and E are such antioxidants that can protect you from bacterial infections and reactive oxygen damage. Vitamin C is shown to play an effective role in the prevention of severe respiratory infections in a different type of research. Collagen production and epithelial viability maintenance are both aided by vitamin C. Vitamin E is a reported fat-soluble component that is necessary for immune system health. It is a potent antioxidant that can lower oxidative stress in the body by trapping reactive oxygen species, and it's also necessary for maintaining immune function, especially in the old aged population (Wong et al., 2021). Vitamin E is indeed engaged in T and B cell accretion and division, along with boosting the functioning of NK cells and APCs, hence influencing immune reaction (Kashir et al., 2021). These data suggest the applicability of vitamin E as a feasible COVID-19 treatment. In a study, it has been proven that tocopherol cannot be that effective single-headedly in comparison to mixed tocopherol (Shakoor et al., 2021).

#### 6.1.3. Vitamin D

SARS-CoV-2 exploits the renin-angiotensin system to obtain access to host tissue, and vitamin D is an important regulator of this system. Vitamin D also affects several immune system pathways, including reducing SARS-CoV-2 appearance and recombination, increasing anti-provocative signalling pathways followed by decreasing pro-inflammatory cytokines along with increasing the production of a natural antimicrobial peptide leading to the destruction of SARS-CoV-2 by activating phagocytic cells (Kumar et al., 2021).

#### 6.1.4. Effects of micronutrients in boosting the immunity of COVID-19 clients

The antioxidant defence relies heavily on the trace mineral selenium. According to epidemiological research, deficiencies in any of these nutritional components can negatively affect immunogenicity and increase the pathogenicity of the virus. According to research, there is a connection between geographic selenium levels and COVID-19 cure rates (Shakoor et al., 2021). T cell numbers are increased, IL-2 cytokine production is increased, NK cell activity is increased, and survival risk is reduced when vitamin E and selenium are combined. Supplementation of Se and vitamin E has been reported to reduce the susceptibility of respiratory organs (Kieliszek & Lipinski, 2020; Wu et al., 2019).

#### 6.1.5. Zinc (Zn)

Zn inadequacy is linked with increased infections and so respiratory system of both children and adults, as well as a higher likelihood are at risk. Plenty of *in vitro* tests has shown that Zn has an antiviral effect against COVID-19. SARS-coronavirus RNA polymerase activity is inhibited by Zn ionophore specifically (Skalny et al., 2020).

#### 6.1.6. Beta-glucan

Beta-glucan, an emulsifiable fiber that derives from yeasts, boosts immunity. In the case of Crohn's disease, asthma, allergies, and other conditions, a "non-starch polysaccharide", glucan has been shown to have health benefits. Glucan can be obtained from cereals, bacteria, molds, and fungi. Beta-glucan is a prospective option for food product development with nutraceutical classification because of its documented health advantages. Beta-glucan could be found in bakery items, milk products, flesh, and liquor, and it can be used to improve the immune system (Mishra et al., 2020).

Instead of these preventive effects, it is also known for its supplementation effects on COVID-19 patients, even though these antioxidant minerals are encouraged to be consumed at sufficient levels. Other nutrients, such as magnesium and vitamin A, have been implicated in the control of COVID-19. Magnesium deficiency has also been assimilated with immune system issues, though the causes remain unknown (Gombart et al., 2020).

#### 6.1.7. Properties of quercetin

Quercetin is an antioxidant with antiviral and anti-inflammatory activities. Quercetin has also been demonstrated to have antiviral properties against both RNA and DNA viruses (Di Petrillo et al., 2022). It lowers the expression of pro-inflammatory cytokines and lung inflammation caused by rhinovirus in mice and inhibits virus entrance and viral-cell fusion. Furthermore, it has been demonstrated that the quercetin metabolite (4′,5-diacetyloxy-3,3′,7-trimethoxyflavone) inhibits picornavirus reproduction by blocking the RNA replicase complex (Wu et al., 2015).

According to research, quercetin-3galactoside binds to viral protease 3CLpro and suppresses its proteolytic activity due to the presence of a hydroxyl group. Furthermore, estradiol's greater potential to influence human genes encoding SARS-CoV-2 targets than testosterone gives a reasonable explanation for the corona pandemic's apparent higher male mortality (Glinskyet al., 2020). Quercetin binds SARS-CoV-2 S-protein at its host receptor area or at the S-protein-human ACE2 interface, preventing virus entrance into cells, as seen in prediction models, showing its therapeutic potential (Safaeian et al., 2016). This prediction is supported by studies that both quercetin and luteolin, a structurally related compound, inhibit SARS-CoV virus infection. Other research has discovered that quercetin in conjunction with vitamin C has synergistic antiviral and immunomodulatory actions against COVID-19 (Smith et al., 2020). Several studies suggest quercetin has potential anti-SARS-CoV-2 properties and could be repurposed as a COVID-19 preventative and treatment option (Shabir et al., 2022).

### 6.2. Utilization of herbs and animal food against COVID-19 infection

Garlic, liquorice, and black cumin are some of the herbs that enhance immunity. Include them in the elderly's diet in the form of tea or by incorporating them into their food. This will not only increase their immunity but also their intestines. In Traditional Chinese Medicine (TCM), herbal treatment is well-known. TCM has a long history and is an important component of the treatment and prevention of certain epidemic diseases (Join et al., 2020).

Herbal medications with immunomodulatory actions may provide patients with a possible preventive treatment option for COVID-19 infection. Several ayurvedic and Traditional Chinese Medicine (TCM) remedies, such as *Tinospora* cordifolia (Willd.) *Miers*, Withania *somnifera (L.)* Dunal, *Scutellaria baicalensis Georgi, Curcuma longa L.,* etc., are efficient during this alarming Coronavirus epidemic. When the COVID-19 pandemic first appeared in early 2020, TCM was demonstrated to be used with over 90% efficacy. Dietary supplements such vitamins and amino acid derivatives, in addition to natural remedies and nutraceutical medications, are crucial in the management of COVID-19. Nutraceuticals can help in prevention of viral invasion, whilst diet can help control inflammation. Functional amino acids, which are found in large quantities in meals derived from animals, are essential for both human and animal health and immunity. Examples of these amino acids include arginine, cysteine, glutamate, glutamine, glycine, taurine, and tryptophan (Chavda et al., 2022).

In order to battle the COVID-19 outbreak brought on by the introduction of the SARS-CoV-2 in the last two years, researchers and the healthcare sectors have been working to repurpose existing medications or develop brand-new, inventive host-directed drugs. This fast effort led to the identification of remdesivir and dexamethasone as possible pharmacological drugs for hospitalised patients. Additionally, most cultures have implemented non-pharmacological preventative measures like public health campaigns to lessen SARS-CoV-2 transmission. But at this time, a lot of people would consume various nutraceuticals and nutritional supplements to bolster their defences.

### 6.3. Benefits of probiotics during viral infection

Probiotics are live microorganisms that provide a health benefit to the host when given in sufficient doses. They can influence immunological function, the creation of antibacterial compounds and organic acids, the integrity of the intestinal barrier, the formation of enzymes, and interactions with the resident microbiota, among other things. Probiotic organisms from the *Lactobacillus* and *Bifidobacterium* genera have been studied for their ability to boost immunological function (Schreck et al., 2017). Although more research is needed to better understand the modulatory mechanisms of the bacteria in these foods, fermented dairy products may be a suitable alternative for improving gut microbiota. *Bifidobacterium* and *Lactobacillus* species are the most often utilised probiotics, followed by *Streptococcus, Enterococcus, Escherichia coli,* and *Bacillus*. Probiotics not only help with gut health, but they also help with system function, and control. Though it is unclear how the gut microbiota protects against respiratory infections via the gut-lung axis. The gut microbiome has been shown to influence systemic immune responses as well as local immunological responses at distal mucosal locations, such as the lungs. *Bifidobacterium* and *Lactobacillus* consumption has been shown to aid in the clearance of influenza virus in the respiratory system (Chong et al., 2019; Vaid et al., 2022).

Probiotics enhance interferon levels, lung mucosal antibodies, NK cell function, and antigen presenting cells (APCs) (Aziz et al., 2016). *Lactobacillus plantarum*DR7 strain has been demonstrated to inhibit pro-inflammatory cytokines TNF- and IFN-, increase anti-inflammatory

**Table 2**
Key Phytosanitary and other technical measures applied to agricultural and food product export (Acaret al., 2006).

| S. No. | Parameters | Phytosanitary Requirement | Refs. |
|---|---|---|---|
| 1 | Food Safety | Hygiene requirementsStorage/Distribution RequirementsPackagingTraceabilityLimits on pesticide residuesLimits on naturally occurring contaminantsLimits on environmental contaminantsLimits on veterinary drug residuesLimits on microbiological pathogensControls on food additivesProduct composition requirementsControls o new food<br>• Inspection requirements | Mc Kenzie et al. (2006) |
| 2 | Plant & Animal Health | QuarantineSurveillanceSanitationFumigation<br>• Traceability | Beckman et al. (2017) |
| 3 | Environmental | Controls on water/environmental contamination<br>Organic production standards<br>Controls on endangered species<br>Environmental protection<br>Biodiversity protection<br>Recyclability requirements | Hallman et al. (2016) |
| 4 | Social | Labour standardsAnimal welfare standards<br>• Fair trade standards | Assoua et al. (2022) |
| 5 | Product Quality Labelling | Compositional standards<br>Grading schemes<br>General labelling<br>Country of origin labelling<br>Nutrition labelling requirements<br>Geographical requirements<br>Controls no claim<br>Labelling of genetically modified foods<br>Domestic content requirements | Santeramo et al. (2018) |

cytokines IL-10 and IL-4, reduce plasma peroxidation levels, and alter the immune system. *Lactobacillus acidophilus* CMCC878 treatment reduced lung damage in mice infected with *Staphylococcus aureus* and *Pseudomonas aeruginosa* by lowering bacterial load and inflammation. Although the mechanism of their immunomodulatory and anti-inflammatory actions in the lungs is unknown. Probiotics have anti-inflammatory and immunomodulatory effects via modulating the NF-B, MAPK, and pattern recognition receptors (PRR) pathways, which reduces Th2 mediated responses while increasing Th1 responses (Ref). Furthermore, they have the ability to prevent bacterial LPS from binding to the CD14 receptor, resulting in a reduction in total NF-B activation and pro-inflammatory cytokine production (Sharma & Im, 2018). Probiotics can be repurposed as prophylactics as well as adjuvants to combat the pathogenesis of COVID-19, given their role in improving the host's innate immune response as well as anti-inflammatory effects, and the fact that gut involvement and enterocytes can be reservoirs of SARS-CoV-2 infection (Hajavi et al., 2019).

### 6.4. Phytosanitary requirements for food products

Concerns about food quality and food safety laws have grown in recent years along the agricultural value chain. Food safety can simply be defined as "what makes your food safe to eat." (Henson et al., 2001). However, there are a few difficulties that make such a description overly simplistic because safety cannot be guaranteed, the word "safe" should be replaced with "safe enough." (The concept of 'acceptable level of risk' should then replace the concept of safety) and quality and safety are not same but correlated. Food safety is a public good, which means that market processes cannot absorb the costs and benefits connected with it, whereas food quality is a private good (though some regulation, such as labelling, is still required). Quality management systems also aid in the resolution of safety concerns. Few parameters for phytosanitary requirements are given Table 2. The term "phytosanitary measure" refers to any action taken to protect plant, animal, or human life or health from threats such as pests, diseases, disease-carrying organisms, or disease-causing organisms; the presence of additives, contaminants, toxins, or disease-causing organisms in foods; or diseases carried by animals, plants, or their products (Aruoma et al., 2006).

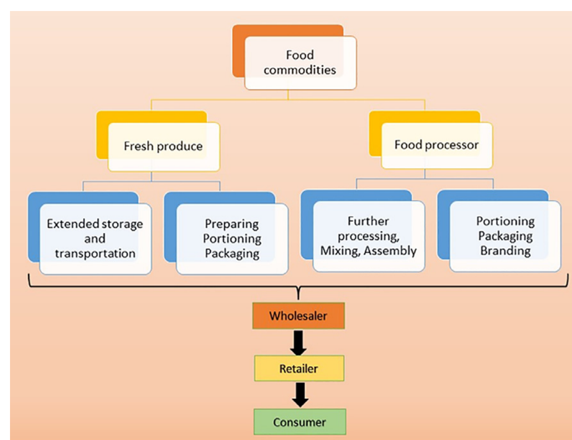


**Fig. 4.** Food chain supply – A trend in technological innovations from food leaving the farm to the consumer use (Aruoma et al., 2006).

In a larger sense, safety also refers to the health of animals (and plants). As a result, food safety and agricultural health are inextricably intertwined. As a result of this, the Agreement on the Application of Sanitary and Phytosanitary Measures (the SPS Agreement) is part of the World Trade Organization's General Agreement on Tariffs and Trade Standards, which tackles the implications of food safety for international trade.

#### 6.1.8. Purpose of sanitary and phytosanitary regulations-

These regulations apply to imported and domestically produced plant and animal goods to protect humans from plant and animal-borne diseases, plants and animals from pests or disease, and countries from the financial costs of pest or disease introduction or dissemination. The journey of food is explained in Fig. 4.

However, as tariff and quantitative limits have been liberalised, there has been rising concern about the impact of additional policies on agricultural and food exports, many of which are not explicitly trade related. Technical restrictions such as food quality and sanitary and phytosanitary (SPS) standards are now commonly accepted to obstruct commerce. Especially in the case of underdeveloped nations. Through the Technical Barriers to Trade (TBT) and SPS Agreements, the Uruguay Round addressed the impact of these limitations on trade (Assoua et al., 2022). However, concerns have been raised those poor nations lack the means to effectively engage in World Trade Organization institutions and hence may be unable to take advantage of the opportunities given by these agreements. The impact of SPS rules on developing countries' capacity to access agricultural and food markets in affluent countries, particularly the European Union (EU). It strives to pinpoint the specific issues that developing nations have in achieving SPS criteria, as well as the extent to which these issues are related to their level of development and the specific needs of developed country markets. The extent to which the SPS Agreement has aided developing countries in overcoming these barriers is investigated, with a focus on the limits that may limit developing nations' effective participation in World Trade Organization institutions (Hallman et al., 2016).

To take full advantage of the opportunities given by international markets, developing nations must resolve food safety concerns and adhere to the SPS Agreement's obligations (Santeramo et al., 2018). There is widespread agreement that farm-to-table science-based (risk assessment) holistic approaches should be used to adopt animal (and plant) health and food safety measures. When the SPS standards of export markets rise, developing countries must maintain and strengthen market access, position industry for long-term competitiveness, mitigate adverse effects on vulnerable people, and improve domestic food safety and agricultural output. LDCs can attain these goals, according to a recent World Bank research, by "adopting a strategic approach to food safety, agricultural health, and trade." For those governments and suppliers who are well-equipped, rising requirements represent an opportunity; for those who are not, they constitute a threat to safety and market access. High-income countries should enhance development aid to poor countries in order to assist them in improving the capacity to formulate and implement the essential plans" (Droppers et al., 2006). This means that such countries must: (a) develop specific plans, programmes, and policies aimed specifically at addressing the challenges of the poor; (b) assess their institutional capacity to meet SPS criteria; and (c) quantify the importance and impact of food safety issues.

*6.4.8. Sanitary and phytosanitary agreements*

Global food safety laws would surely aid in ensuring fair trade rivalry between countries while also ensuring that all populations have access to the same level of food safety. This was one of the guiding principles of the Uruguay Round of Multilateral Trade Negotiations, which resulted in the World Trade Organization (WTO) being established in 1995, with a number of agreements such as the Agreement on SPS Application and the Agreement on Technical Barriers to Trade (TBT). The Agreement on the Application of Sanitary and Phytosanitary Measures (the "SPS Agreement") became effective with the establishment of the World Trade Organization (WTO, 1995). The SPS agreement was designed to address concerns about food safety. Despite the fact that the original General Agreement on Tariffs and Trade (GATT) in 1947 imposed some restrictions under Article XX(b), it was claimed that many countries were utilising food safety concerns to justify, maintain, or create trade barriers against imported commodities. As a result, the SPS Agreement covers a wide range of activities relating to food safety as well as animal and plant health. As a result, the SPS Agreement covers all sanitary and phytosanitary measures that could have an impact on international trade. Import market consumers need quality and safety, therefore exporters must deliver. As a result, international trading norms exist to ensure that public standards are enforced fairly and equally to both native and imported goods (McKenzie & Hathaway, 2006).

As a result, countries must make their regulations public and provide a method for responding to questions from trading partners. Even if the measures themselves differ, member nations must recognise that SPS measures from another country are equal if they result in the same level of public health protection. Both domestic and imported items should have the same level of health protection. Regulations should be written in such a way that they cannot impose requirements without a scientific foundation for risk reduction. Within an exporting country, the concept of pest- or disease-free zones is recognised. Exports from such places may be permitted, even if the illness or pest is still present in other parts of the exporting country. Countries may choose a risk standard that is not the same as the international standard (Schnöller, 2006). Countries have the option of using a risk standard other than the international norm. Individual nations are unwilling to agree to universal worldwide standards for all hazards, as evidenced by this. There is a well-defined process in place for quickly settling international conflicts. The only thing the dispute resolution panel is supposed to say is if the SPS measures in question have a scientific basis and are applied consistently (Siméon, 2006).

Member countries also agree that common SPS measures are desirable. Fresh fruits and vegetables can harbour a variety of pests that, if not treated effectively, can be introduced and spread widely, inflicting economic loss in pest-free areas. Fruit-importing countries may require that fruits and vegetables from areas where pests represent a risk to agriculture be treated according to treatment regimens that they have approved. Any import usually requires individual treatment programmes for distinct pest/commodity combinations (Slorach, 2006). As a result, a potential fruit and vegetable exporting country may be required to undergo testing to ensure that their exports are phytosanitary secure. Phytosanitary laws in fruit-importing countries such as Australia, Japan, New Zealand, South Korea, and the United States effectively turn into technical barriers that are difficult to overcome on a case-by-case basis. As a result, broad-spectrum phytosanitary treatments are urgently needed to meet the phytosanitary criteria of importing countries based on internationally agreed-upon protocols, and ionising radiation has shown promise as one such therapy. Irradiation has yet to be approved in key import markets such as the European Union, Japan, South Korea, and Taiwan (Unnevehr & Hirschhorn, 2000).

## 7. Conclusion

The immune system is the prime factor in illness management. Treatments for viral diseases, on the other hand, remain a major issue due to the virus's genetic material's ability to easily reorganize themselves to produce new antigens that can avoid the host body. Nutritional techniques for increasing immunity should be researched for infectious diseases such as COVID-19, where no medical treatments or therapy are now accessible and the time of the frightening situation's termination is uncertain. Immuno-nutrition is very crucial in modulating the activity of the immune system or the implications of immunity activation by specific nutrients or meals. As a result, immuno-nutrition and lifestyle changes are critical in dealing with potentially fatal viruses like SARS-CoV-2. A few vitamins (Such as $B_6$, $B_{12}$, C, E) and trace elements (Such as Zn, Cu, Mg, Se, Fe) have been represented to play essential functions in boosting the human immune system and reducing infection possibility through research and analysis of persons with deficiencies. It will be difficult to meet the recommended calorie and micronutrient intakes.

This review of boosting immune system techniques could be referred for the treatment of COVID-19 infected patients. Immune system activities and functions can provide useful information for immune system development. The research on COVID-19 treatment could be the focus of future research and this would be a great achievement If obstacles in treatment could be surmounted. Finally, because there is no FDA-approved treatment for COVID-19, nutrition is the only option (e.g., dietary advice) to increase the immune system should be investigated and advised.

## Animal consent statement

The authors declare that they have not used any animal or human that could have appeared to influence the work reported in this paper.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Data Availability

No data was used for the research described in the article.


## Acknowledgements

Authors are thankful to Integral University for providng the manuscript number IU/R&D/2023-MCN0001830.


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