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Review article

Immunity boosting roles of biofunctional compounds available in aquafoods: A review

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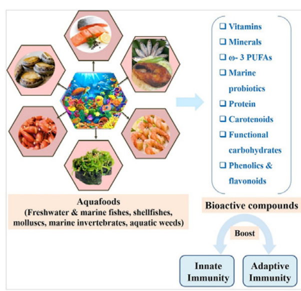
HIGHLIGHTS

- Various bioactive compounds are available in diverse aquafoods.
- Aquafoods are rich in vitamins, minerals, amino acids, ω-3 PUFAs, and pigments.
- These compounds enhance immunecompetence and immunomodulation.
- Boosting immune system is an effective way to combat infectious diseases.

GRAPHICAL ABSTRACT



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ABSTRACT

Aquafoods are diverse and rich in containing various health functional compounds which boost natural immunity. In this manuscript, the contents of biofunctional compounds such as vitamins, minerals, protein and amino acids, ω-3 polyunsaturated fatty acids, and pigments, etc. in various aquafoods like fishes, molluscs, crustaceans, seaweeds etc. are reported. The functional roles of those compounds are also depicted which enhance the immunecompetence and immunomodulation of the consumers. This paper provides an account of the recommended daily dietary intake level of those compounds for human. Those compounds available in aquafoods are recommended as they fight against various infectious diseases by enhancing immunity. Available reports on the bioactive compounds in aquafoods reveal the immunity boosting performances which may offer a new insight into controlling infectious diseases.

1. Introduction

Aquatic environment is an array of diverse organisms (fish, shellfish, marine invertebrates, and aquatic weeds) which are rich in numerous health beneficial nutrients and compounds (Atef and Ojagh, 2017). Aquafoods ensure a range of advantages such as improve public health, economy and social welfareness (Stentiford et al., 2020). Aquafoods are rich in protein, peptides and amino acids, vitamins, minerals, ω-3 PUFAs, probiotics, polysaccharides, and bioactives etc. are reported to stimulate immunity against viral infections, influenza and so on (Yao et al., 2020; Wu et al., 2019). Presently, the attention is given to explore the functions of bioactive compounds from aquatic organisms which boost immunity (Figure 1). The immune system of human body consists of innate and adaptive immunity. It is regulated by various biopotential compounds such as vitamins, minerals, proteins, polyunsaturated fatty acids, probiotics, and so on (Figure 2). The innate immunity is first defense

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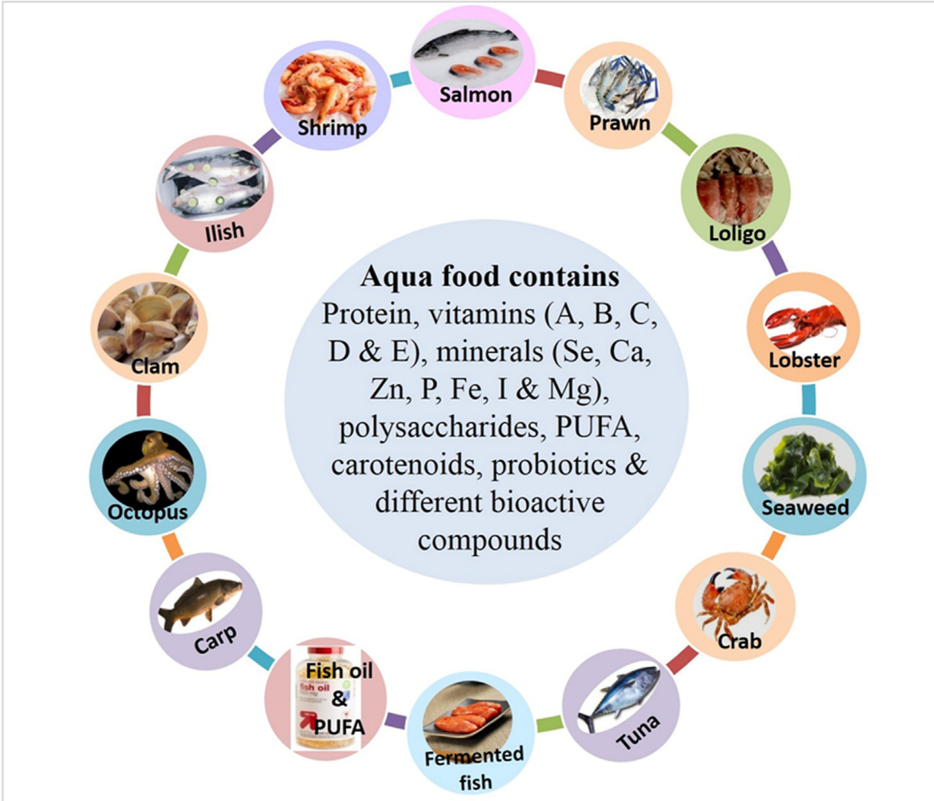

Figure 1. Various bio-potential compounds such as vitamins, minerals, proteins, polysaccharides, polyunsaturated fatty acids (PUFAs), carotenoids, probiotics, etc. are available in aquatic organisms which boost our immunity. Abbreviations: Se: Selenium; Zn: Zinc; Mg: Magnesium; Ca: Calcium; P: Phosphorus; Fe: Iron, I: Iodine.

mechanism against any pathogen and microorganisms. The innate immunity process is comprised of (i) Physical obstructions such as skin, hair, mucus, the gastrointestinal truct, the endothelial cell stratum in the respiratory tract, nasopharynx, cilia, and eyelashes (ii) Biochemical defense mechanisms (saliva, tears, sweat, secretion, mucus, gastric acid, and biles (iii) Cellular responses by phagocytic cells-monocytes and macrophages, natural killer (NK) cell, mast cell, dendritic cells, neutrophils, eosinophil, and basophil (Maggini et al., 2018). The innate immune system instantly responds to invading microorganisms, but the main weaknesses are non-specific and absence of memory effect. It is a non specific defense mechnisms that is activated immediately or within hours of antigen penetration in the body. The adaptive immune system is stimulated to terminate the antigen when the innate immunity cannot remove the antigen over a short period. The adaptive immunity consists of T and B cell mediated immunity and humoral factors lymphocytes. Cytotoxic T cells contain CD8+ receptor, involved in antigen recognition and killing of infected damaged/tumour cells. Helper T cells (Th) contain CD4+ receptor, plays important role in co-ordination of immune response (Gombart et al., 2020). Different subtypes of Th cells produce different cytokines which are responsible for immune responses. Interferon- γ (IFN-γ) and Interleukin-2 (IL-2) are produced by the Th1 cells which are potential for antiviral immune response. Other subtypes Th2 produces cytokines IL-4, IL-5, and IL-13 which are involved in antibody production. Th17 cells produce IL-17A, IL-17F, and IL-22 which fight against bacteria and fungi (Childs et al., 2019). Other B lymphocytes cells are responsible for five types of Immunoglobulin (Ig: IgM, IgD, IgG, IgA and IgE) production. IgA found in serum and mucosal surfaces prevent viral and bacterial infections. B cells are controlled by the cytokines secreted from Th cells (Childs et al., 2019; Crooke et al., 2019).

The function of these immune cells depends upon adequate and appropriate nutrition make up from dietary sources or from body store. The optimal nutrition supports the function of immune cells and initiates effective and rapid response against pathogens and prevents chronic inflammation (Figure 3). Some micronutrients such as vitamin A, C, D, E, zinc, and some amino acids showed very special roles for the improvement, development, and maintenance of active immunity process during the whole life cycle or during chronic inflammation. The micro nutrient deficiencies and reduced number of T cells in older people altered the function of T cells. The immune function of older one and immune deficient people can be improved by restoring nutrients such as protein, peptides, polysaccharides, vitamins A, B2, B6, B12, folic acid, C, D, E, iron, calcium, magnesium, selenium, PUFAs, phenolics, carotenoids, probiotics and other bioactive compounds by dietary supplements (Atef and Ojagh, 2017; Şanlier et al., 2019; Suraiya et al., 2018, 2019). Even, the roles of healthy nutrition are more important for defensing various infectious diseases compared to nutritional disorders. Additionally, poor maternal nutrition and related impaired fetal growth are strongly correlated with neonatal death from pneumonia, sepsis, and diarrhoea. Malnourishment is a well reported risk factor for tuberculosis and nutrient deficiencies, such as vitamin A deficiency is considered to be linked with diarrhea severity and malaria disease in some populations (Rohr et al., 2019). In this case aqua-based resources could be promising immune enhancing foods to improve immunity against various infectious diseases. Therefore, this paper describes an overview of the biofunctional compounds content in aquatic organisms, their recommended daily dietary intake, and immunity boosting roles to fight against infectious diseases in human body.

2. Immune functions of aquafood compounds

The immunomodulatory roles of bioactive compounds available in aquafoods are summarized in Table 1.

2.1. Protein, peptides and amino acids

The protein of aquatic animals is considered better than terrestrial one due to containing some unique amino acids and easy digestability.

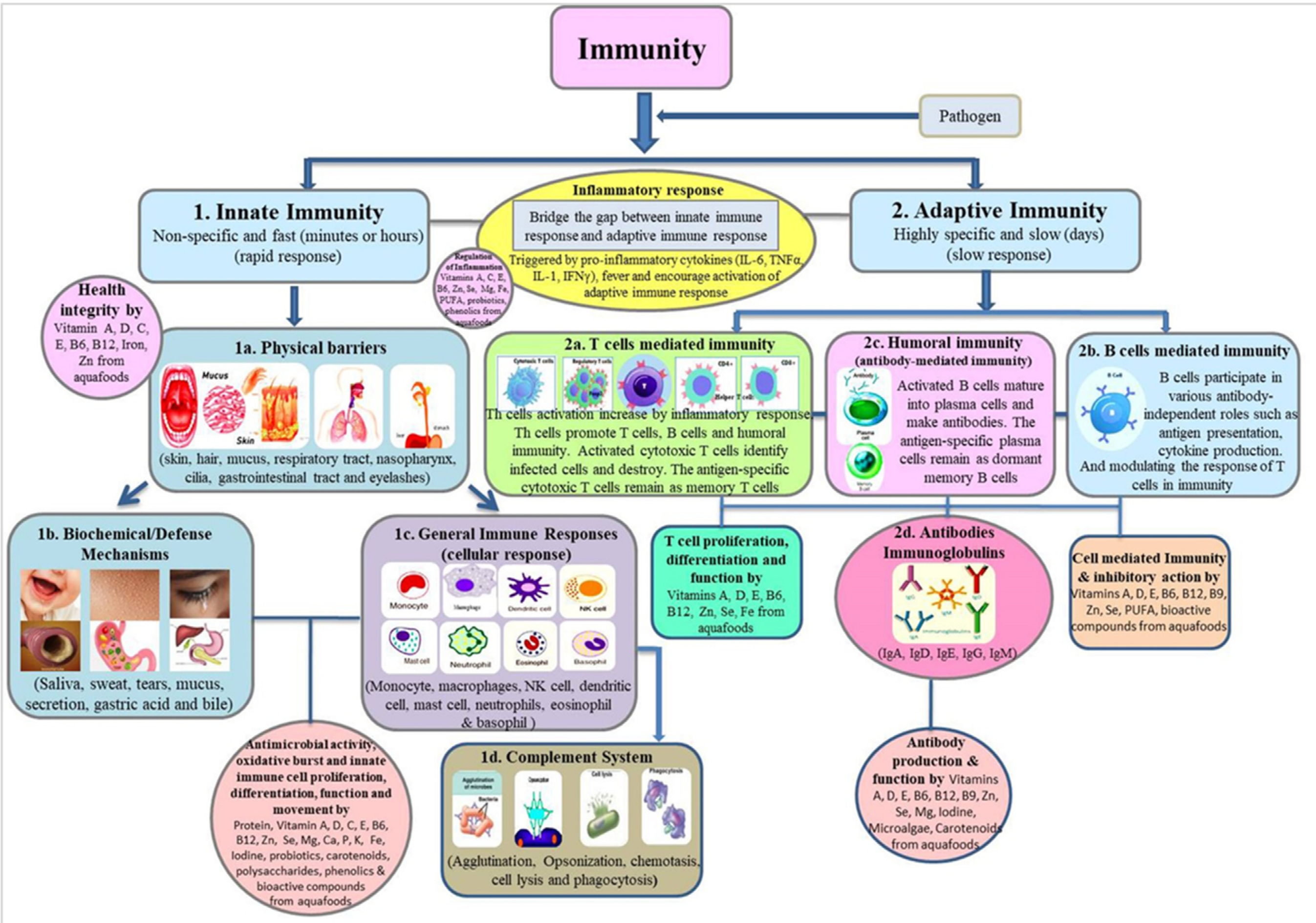

Figure 2. Schematic diagram of an overview of human immune system. Body immunity controlled by different immune cells and components. The contributions of micro and macro nutrients from aquafoods on boosting immunity to fight against pathogens. Abbreviations: IL-6: Interleukin 6; TNFα: Tumor necrosis factor alpha; IL-1: Interleukin 1, IFNγ: Interferon gamma; Th cells: Helper T cells; NK cell: Natural killer cells; Ig: Immunoglobulin, Se: Selenium; Zn: Zinc; Mg: Magnesium; K: Potassium; Ca: Calcium; P: Phosphorus; Fe: Iron.

Aquatic proteins have high nutritional value rich in essential amino acids (Table 2), specially methionine and lysine. Many bioactive peptides from fish, fish by-products, marine invertebrates, and fermented aqufoods exhibited different biological activities such as cholesterol and blood pressure lowering effect, antimicrobial, and antioxidant activities (Atef and Ojagh 2017; Yao et al., 2020; DarewiCz et al., 2016). Amino acids of aquatic organisms perform important role in boosting immune response by controlling the activation of natural killer cells, T lymphocytes. B lymphocytes, and macrophages, lymphocyte proliferation, antibody production, gene expressions, and cytokines production (Khalili Tilami and Sampels, 2018). The dietary supplementation of specific amino acids (arginine, cytosine, and glutamine) to people with malnutrition and infectious disease improve the immune status and reduce mortality rate (Li et al., 2007). During inflammation, comparatively high protein intake is required to stimulate the synthesis of specific proteins, compensate depleted amino acids (e.g., arginine or glutamine), modulate immune functions, redox unbalance, and counteract insulin resistance. The results have been shown that fish protein hydrolysates (high in arginin content) reduced the production of Tumor Necrosis Factor-α (TNF-α). Arginine also inhibits the production of superoxide anions by nitric oxide synthase. The synergistic effects of fish protein hydrolysates and ω-3 PUFAs reduced the expression of TNF-α compated to fish protein hydrolysates or ω-3 PUFAs individual administration (Rudkowska et al., 2010). Therefore, glycine in fish protein hydrolysates suppresses the expression of pro-infammatory cytokine IL-6. Amino acid taurine from fish by-products represses the production of IL-1β, TNF-α and IL-6 (Lund, 2013). The host defence mechanisms are collapsed by protein imbalance. Both very high (>60%) and low protein (<20%) diet were exhibited to damage phagocytic activity and IL-2 production (Venkatraman and Pendergast, 2002). Dietary protein supplement gave efficient results against typhoid fever and othe infections (Kang et al., 2020). The hydrolysis of fish or fish by-products produces different types of bioactive peptides with significant health benefits. Fermented fish products are a good source of peptides and amino acids. Fermentation of carp fish heads (rohu and catla) with lactic acid bacteria produced antioxidant peptides (Murthy et al., 2014). Patients with COVID-19 are recommended to ingest food comprising or stimulating the synthesis of melatonon and serotonin. Aquafoods rich in various amino acids including tryptophan are precursor of melatonon and serotonin. A recently study shown that, 20 marine fish proteins were hydrolysed by gastrointestinal enzymes which contained a large number of active peptides and oligopeptides suggested to use as potential compounds to fight against COVID-19 and anxiety (Yao et al., 2020).

2.2. Vitamins

2.2.1. Vitamin A

The recommended daily dietary allowance of vitamins and the contents of vitamins in fishes and shellfishes are presented in Tables 3 and 4, respectively. Marine oily fishes such as salmon, cod, mackerel, tuna, herring, etc. are good sources of vitamin A. Vitamin A deficiency causes nyctalopia (night blindness), xerophthalmia (eye dryness), and in severe

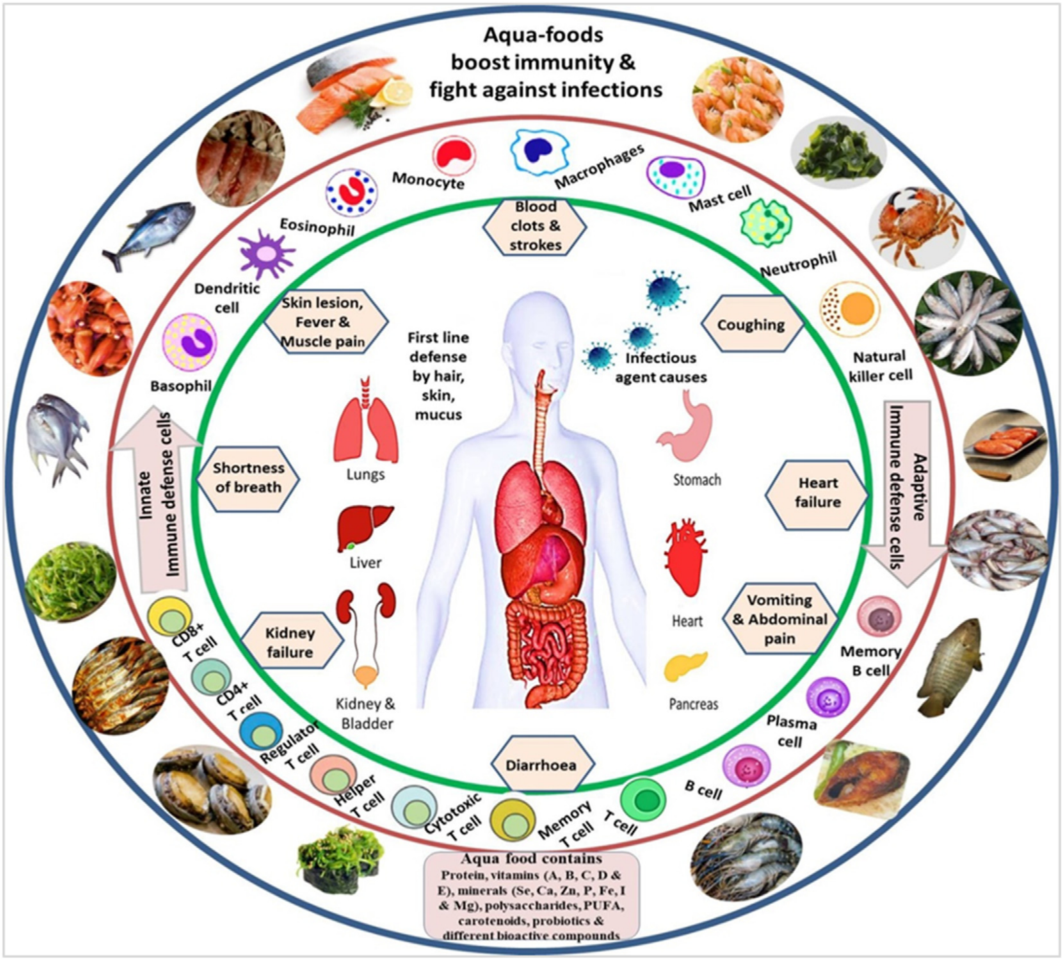

Figure 3. Diagram represents the immunity boosting role of aqufoods to fight against infectious diseases. Microbial infections affect different organs of human and cause disfunction. Micro and macronutrients of aquafoods modulate innate and adaptive human immune defense system to fight against the pathogen. Abbreviations: Se: Selenium; Ca: Calcium; Zn: Zinc; P: Phosphorus; Fe: Iron; I: Iodine; Mg: Magnesium.

case keratomalacia. Vitamin A regulates the function of different cells in immune system. It keeps the respiratory system healthy and prevents infections from various viral diseases. It is also known as anti-inflammatory vitamin (Sharma, 2020). Vitamin A deficiency causes impairment of phagocytes, T, and B cells activity. NK cells, neutrophils, macrophage, and lymphocytes activity have also been reduced due to vitamin A deficiency. It is reported that vitamin A supplement in deficient host improves immune function and increases resistance to infections. The level of serum immunoglobulins such as IgA and IgG is improved by vitamin A supplementation and also reduced the secretion of inflammatory cytokines. Low level of vitamin A causes diarrhoeal diseases and respiratory problems in children. The deficiency of vitamin A causes minimal epithelial changes when it is complicated by infectious agents. Vitamin A deficiency causes impairing of mucosal barriers, Th1 and Th2 cell mediated immune response, especially antibody-mediated response (Goldrosen and Straus, 2004). In children, the recovery from measles is also improved by supplementation of vitamin A and decreased duration of illness and mortality rate. Low concentration of vitamin A in serum increases viral disease HIV progression (Sharma, 2020). The results showed that the children of 2–8 years posses improvement of immune response against influenza virus after supplementation of vitamin A (Jayawardena et al., 2020).

2.2.2. Vitamin B

Many fishes and shellfishes including seabass, mackerel, crustaceans, molluscs, shrimps, cuttle fish, etc. are rich sources of vitamin B complex. Marine salmons and freshwater trouts contain variety of vitamin B such as B1, B2, B3, B5, B6, B9, and B12. Mackerel, tuna, herrings, monkfish, clams, oysters, mussels, lobster, octopus, loligo, and fish roe are rich sources of vitamin B12 (Bourre and Paquotte, 2008). It has been shown that the dietary vitamin B12 from fish is more bioavailable than from meat and eggs. Improvement of blood plasma level of B12 was related with dietary intake of fishes and shellfishes. Vitamin B is required for the development of red and white blood cells, DNA synthesis, and neurological functions. Vitamin B2, B6, and B12 regulate inflammations and maintain the immune system working properly (Saeed et al., 2016; Maggini et al., 2018).

Vitamin B6 and B12 play significant role in cytokine production and maintain or enhance NK cell cytotoxic activity in innate immunity (Wu et al., 2019; Maggini et al., 2018). In case of adaptive immune response, vitamin B6 was required for the synthesis of amino acids, cytokines and antibodies, and its metabolism (Saeed et al., 2016). The maturation, proliferation, and differention of lymphocytes are dependent on vitamin B6. Vitamin B6 maintains Th1 immune response and inhibits cytokine-mediated activity of Th2. Lymphocytopenia, an extremely low concentration of lymphocyte (a white blood cell performing important roles in immune system) and response of antibody are reduced due to deficiency of vitamin B6. Vitamin B12 enhances activity of cytotoxic CD8+ T cells, NK cells, and modulates cellular immunity. B12 deficiency causes delayed in T cell proliferation and lowered the immune responses. B12 facilitates the production of T lymphocytes and performs vital role in humoral and cellular immunity. The production and metabolism of antibody is dependent on vitamin B12 (Saeed et al., 2016).

Table 1. Immunomodulatory roles of bioactive compounds from aquafoods

Bioactive compounds	Functions	References
Protein, peptides, and amino acids	* Activate B lymphocytes, T lymphocytes, macrophages and natural killer cells. * Boosting immune response by inducing lymphocyte proliferation, antibody production, gene expressions, and cytokines production	Khalili Tilami and Sampels, 2018; Lund, 2013; Rudkowska et al., 2010; Yao et al., 2020
Vitamins (A, B, C, D, and E)	* Vitamin A enhances phagocytes, T cells, B cells activity and antibody-mediated response. It also induces the function of NK cells, neutrophils, macrophage and lymphocytes activity. * Vitamin B2, B6, and B12 regulate inflammations and maintain the immune system. Vitamin B6 and B12 play significant role in cytokine production and maintain NK cell. Vitamin B12 enhances activity of cytotoxic CD8+ T cells, NK cells, and modulates cellular immunity. B12 regulates T cell proliferation and immune responses. * Vitamin C is involved in proliferation, movement, and function of neutrophils, monocytes, and phagocytes. It also enhances NK cell activities, phagocytosis, microbial killing, and neutrophil chemotaxis. * Vitamin D promotes the chemotactic and phagocytic capacity of macrophages. It stimulates cell proliferation and cytokine production. Activated vitamin D produces endogenous antimicrobial peptides in epithelial cells, monocytes, and neutrophils. * Vitamin E enhances cytotoxicity of NK cells and cytokine IL-2 production. Vitamin E deficiency affects the functions of both T and B cells and weakens both humoral and adaptive immunity. It also increases proliferation and function of T cells, ratio of CD4+ T cells and CD8+ T cells, and decreases oxidative stress.	Sharma, 2020; Saeed et al., 2016; Maggini et al., 2018; Wu et al., 2019; Wu et al., 2019; Gombart et al., 2005; Kalinski, 2012; Saeed et al., 2016
Minerals (Iron, Iodine, Magnesium, Selenium, Calcium, Potassium, Phosphorus & Zinc)	* Iron plays essential role in transportation of oxygen throughout the body. Iron supplementation has a positive effect on the levels of cytokine IL-6 in serum. It is important for differentiation and proliferation T cells. It also helps to maintain the ratio between T helper cells and cytotoxic T cells. * Iodine acts as fuel to maintain metabolic activity in the body. It induces the production of thyroid hormone which influences normal growth, metabolism, and oxygen consumption of cells and central nervous system. It increases the movement of granulocytes into the areas of inflammation, increases IgG production in human lymphocytes and ultimately improves human immune functions. Iodine also improves the process of phagocytosis by granulocytes to kill microorganisms. * Mg helps to bind antigen in macrophage, regulate lymphocyte activation, apoptosis, and antibody dependent cytolysis * Selenium enhances the differentiation and proliferation of T cells, and increases the number of T helper cells. Selenium helps to maintain antibody levels of the body. * Ca is essential for metabolism and intracellular signaling. Intracellular calcium regulates immune functions such as cell proliferation, cytokine production, and cytokine receptor expression. Calcium and phosphorus are important for brain functions and strengthen body immune system. * Zinc supports the immune system working properly and wounds healing. Zinc aids in binding tyrosine kinase to T cell receptors in intracellular level which is a prerequisite for T lymphocyte growth and activation. Zinc also displayed to induce the growth of Treg cell population and inhibit pro-inflammatory Th17 and Th9 cell differentiation.	Arshad et al., 2020; Saeed et al., 2016; Venturi and Venturi, 2009 Maggini et al., 2018; Childs et al., 2019; Maggini et al., 2018
Fish oil and ω-3 polyunsaturated fatty acids	* Omega-3 PUFAs show antiarrhythmic functions, anti-inflammatory effects, reduce platelet aggregation, reduce blood pressure, vasodilation, plaque stabilization, and reduce triglyceride levels in bloods. Shows the capacity to hind the formation of inflammatory mediators such as pro-inflammatory cytokines (IL-1b, TNF-α, IL-6), eicosanoids (PGE2, leukotrienes), chemokines (IL-8, MCP-1), platelet activating factors, adhesion molecules (ICAM-1, VACM-1, selectins), ROS, and RNS.	Haq et al., 2018; Haq et al., 2020; Goldrosen and Straus, 2004.
Marine probiotics and fermented aquafoods	* Probiotics induced the production of pro-inflammatory cytokines to assist immune function against infection. * Fermented aquafoods are responsible for immune system enhancer, counter inflammation, and stimulate the proliferation of human white blood cells, exhibit adequate immunomodulatory and anti-inflammatory activity.	Kekkonen et al., 2008 Thongthai and Gildberg, 2005; Pyo and Oh, 2011; Mun et al., 2017; Suraiya et al., 2019
Carotenoids	* Carotenoids prevent oxidative stress, control central nervous system, and enhance body immunity. It also reduces chronic inflammation and fight against cancer, eye disorders, rheumatoid arthritis, cardiovascular disease, and neuro degenerative diseases.	Hughes et al., 2000; London, 2010); Abe et al. (2007); Ví lchez et al., 2011.
Bioactive phenolic and flavonoid compounds	* Phenolics and flavonoids have been demonstrated antioxidant, anti-obesity, anti-inflammatory, and immunomodulatory properties. Marine brown algae stimulate the mononuclear phagocytic system, activate dendritic cells, promote the tumor-specific Th1 responses, increase	Bahar et al. (2016); Suraiya et al., 2019; Zhang et al., 2019.

(continued on next page)

Table 1 (*continued*)

Bioactive compounds	Functions	References
	the CD4+/CD8+ T lymphocyte ratio, and enhance cytotoxic T lymphocyte responses.	
Functional carbohydrates (oligosaccharides and polysaccharides) from aqufoods	* Polysaccharides from seaweeds showed variety of pharmaceutical properties such as antiviral, antioxidant, and anti-inflammatory properties. Different types of polysaccharides from seaweeds exhibit strong immunomodulatory activity by NF-κB-dependent immunocyte maturation and differentiation.	Islam et al., 2013; Elaya Perumal and Sundararaj, 2020; Fang et al., 2015; Fu et al., 2019; Sansone et al., 2020
Marine invertebrates	* Compounds isolated from marine invertebrates possess anticancer, anti-helminthic, antihypertensive, antifungal, antiviral, antibacterial, and immune modulatory properties. * Sea cucumber protein hydrolyzate demonstrates not only the reduction of ROS accumulation in cells but also directly scavenge free radicals.	Odeleye et al., 2020; Suleria et al., 2015). Guo et al., 2020.
Microalgae	* Spirulina showed potential results against viral infections. Marine microalgal polysaccharides, naviculan from *Navicul adirecta*, and other A1 and A2 from dinoflagellate *Cochlodinium polykrikoides* exhibited antiviral activities against HIV-1 and influenza virus type A. The green microalga increases the production of immunoglobulin (IgA, IgG, and IgM) by stimulating T-helper (Th) cells. It also increases the immune response by NK cells and decreases stress related inflammation.	Yakoot and Salem, 2012; Liu et al., 2020; Raja and Hemaiswarya, 2010; Sansone et al., 2020

2.2.3. Vitamin C

Aquatic (both freshwater and marine) weeds are important source of vitamin C. *Alternanthera philoxeroides* and *Ipomoea aquatica* (Spermatophyrta) leaves contain vitamin C of 50 mg and 238 mg/g of fresh weight (Yang et al., 2014). Brown and green seaweeds contain higher amount of vitamin C than red seaweeds. The average levels of vitamin C in green and brown algae vary between 500–3000 mg/kg of dry weight (which is comparable with peepers, lemon, and parsley), while red algae contain average 100–800 mg/kg dry weight (Burtin, 2003).

Vitamin C is involved in proliferation, movement, and function of neutrophils, monocytes, and phagocytes. It enhances NK cell activities, phagocytosis, microbial killing, and neutrophil chemotaxis (Wu et al., 2019; Maggini et al., 2018). It reduces tissue damage and involves in apoptosis and cleans the spent neutrophils from the infection sites by macrophages (Carr and Maggini, 2017). The antimicrobial effect can be improved by intaking high levels of vitamin C. It has role in cytokine production and increase serum complement proteins. It maintains redox homeostasis within cells and protects against reactive nitrogen species (RNS) and reactive oxygen species (ROS) during oxidative burst (Maggini et al., 2018). Vitamin C perform crucial roles in production, differentiation, proliferation, and maintaining the activity of lymphocytes and cytotoxic T cells, and increase antibody production. Vitamin C deficiency causes oxidative damage and delayed in wound healing. It not only stimulates phagocytic but also protects leukocytes and lymphocytes from oxidative stress. Severely ill patient can recover soon by using high dose of vitamin C (Hemilä and Chalker, 2019). It strengthens the immune defence system, stimulates the intestinal absorption of iron, and restores Vitamin E. Vitamin C was used to decrease the prevalence of general cold, which is mostly occurred by viral infections (Jayawardena et al., 2020). Enhakced production of interferon-α/β is an essential factor for the antiviral immune response against influenza A virus (H3N2) (Himaya and Kim, 2015). Jayawardena et al. (2020) recommended to intake vitamin C for enhancing immunity against viral infections, emphasizing COVID-19.

2.2.4. Vitamin D

Seafoods such as cod, salmon, sardines, herring, mackerels, tuna, halibut, channel catfish, flounder, cod, oyster, shrimp, clams, and fish caviar etc. are rich in vitamin D (Table 4). The usual functions of vitamin D are known to regulate the bone health and calcium homeostasis. In addition to extra-skeletal functions, vitamin D activates the hydroxylases enzymes and vitamin D receptors (VDR) present in the immune cells (Wu et al., 2019). The active form of vitamin D (Calcicitrol, 1,25(OH)$_2$D3) stimulates vitamin D receptor (VDR) which increases both the adaptive and innate responses (Wu et al., 2019; Gombart et al., 2005). The functions of different immune cells (monocytes, macrophages, dentritic cells, etc.) are influenced by vitamin D. Active form of vitamin D stimulates the phagocytic and chemotactic ability of macrophages. It not only stimulates cell proliferation and cytokine production but also helps to fight against microorganisms. Activated vitamin D has the ability to produc several kinds of endogenous antimicrobial peptides (cathelicidin and defensins) in epithelial cells, monocytes, and neutrophils. These antimicrobial peptides play crucial role to modify intestinal microbiota to a healthier composition and keep integrity of gut epithelial barrier, renal epithelial barrier, and protect lungs from infection. It enhances elimination of invading pathogens such as bacteria, fungus, and virus. Vitamin D deficient diets are responsible for increasing permeability of gut epithelial which causes both acute and chronic gut inflammation. Vitamin D deficiency causes the reduction of lymphocytes, thus affect immune response. It has impact on the function of T-cells by modulating differentiation of CD+4 T cell into regulatory T (Treg) cells, Th1, Th2, and Th17 (Wu et al., 2019). The clinical studies have showed that the supplementation of vitamin D exhibited promising results against several diseases such as HIV, tuberculosis, hepatitis C, and respiratory tract infections. Similar results were also reported that vitamin D improved immune response and fought against viral diseases like influenza A and B, parainfluenza 1 and 2, and respiratory syncytial virus (Jayawardena et al., 2020). Moreover, vitamin D defends respiratory tracts, kills envelop viruses by stimulation of defensins and cathelicidin, and reduces the production of proinflammatory cytokines; thus reduces the risk of cytokine which leads to pneumonia.

2.2.5. Vitamin E

Atlantic salmon, rainbow trout, snails, crayfish, shrimps, abalone, and octopus are good sources of Vitamin E. Vitamin E is an efficient antioxidant for skin and maintains heart, circulatory, and nervous system. Vitamin E is a fat soluble antioxidant which shields cell membranes from the damage caused by scavenging free radicals and maintains the integrity of epithelial barriers (Wu et al., 2019). It also protects lipid of cell membrane from peroxidation. Incase of immunity, Vitamin E enhances cytotoxicity of NK cells and cytokine IL-2 production. Vitamin E deficiency affects the functions of both T and B cells and weakens both humoral and adaptive immunity. Supplementation of vitamin E increases proliferation and function of T cells, ratio of CD4+ T cells and CD8+ T cells, and decreases oxidative stress. The production of prostaglandin E_2 (PGE2), a naturally occurring prostaglandin generated by macrophages and involveded in T-cell supression is decreased by vitamin E. PGE2 has negative effects on innate and adaptive immunity which inhibit T cell proliferation, cytokine IL-2 production, and expression of IL-2 receptor (Kalinski, 2012). It also increases the number of antigen-experienced memory T cells (Saeed et al., 2016). It is necessary to supplement vitamin E in elderly people to improve the proliferation and function of lymphocyte, ultimately overall immunity.

Table 2. The contents of different essential amino acids (g/100 g protein) available in different aquafoods.

Species	Valine	Leucine	Isoleucine	Lysine	Methionine	Phenylalanine	Threonine	Tryptophan	References
Saccostrea cuccullata	2.1	3.5	2.4	4.1	1.1	-	2.7	-	Moniruzzaman et al. (2021)
Pila globosa	1.6	2.6	2.4	3.1	0.8	-	2.1	-	
Crassostreavirginica	2.4	3.5	2.3	4.2	1.1	-	2.9	-	
Finfish	5.8	8.5	5.3	9.8	2.9	4.2	4.8	1.1	Ariño et al. (2013)
Crustaceans	4.8	8.6	4.6	7.8	2.9	4.0	4.6	1.1	
Molluscs	6.2	7.7	4.8	8.0	2.7	4.2	4.6	1.3	-
Horse mackerel	0.65	0.83	0.58	0.96	0.37	0.47	0.44	-	Erkan et al. (2010)
Garden snail (*Helix aspersa*)	0.71	0.61	0.46	0.72	0.43	0.36	0.45	-	Çagiltay et al. (2011)
Rainbow trout (*Oncorhynchus mykiss*)	0.60	1.16	4.63	1.41	0.27	0.65	0.75	-	Nurhan (2007)
Sturgeon (*Huso huso*)	4.16	9.51	5.03	8.40	1.11	4.61	5.37		Kaya et al. (2008)
Commerson's anchovy (Stolephorus commersonii)	6.95	7.99	0.40	8.66	1.44	3.74	5.50	1.72	Sankar et al. (2013)
Mullet *(Mugil cephalus)*	5.42	8.89	4.78	10.13	2.86	3.96	4.52	0.71	Kumaran et al. (2012)
Codium fragile	1.41	0.73	0.40	0.55	0.95	0.48	0.59	0.39	Ortiz et al. (2009)
Gracilaria chilensis	0.77	0.45	0.80	0.66	1.88	1.09	0.64	0.39	
Macrocystis pyrifera	1.14	0.34	0.51	0.32	1.11	0.59	0.74	0.43	
Giant River-Catfish (Sperata seenghala)	6.07	9.12	6.37	0.93	1.74	4.31	9.21	1.30	Mohanty et al. (2012)
Crab (*Chionoecetes opilio*)	1.38	1.58	0.96	2.07	0.48	1.3	1.58		Vilasoa-Martínez et al. (2007)
Mussels (*Mytilus galloprovincialis)*	0.66	0.96	0.59	0.1.05	0.25	0.84	-	0.68	Şengör et al. (2008)
Oyster (*Crassostrea madrasensis*)	2.6	2.0	4.5	14.3	4.7	4.1	12.3	-	Asha et al. (2014)
Shrimp (*Aristeus virilis*)	1.22	1.96	0.84	2.03	0.67	0.95	1.21		Karuppasamy et al. (2013)
Spirulina platensis	7.1	9.8	6.7	4.8	2.5	5.3	6.2	0.3	Lum et al. (2013)
Oysters (*Crassostrea madrasensis*)	0.0061	0.006	0.002	0.006	0.005	0.009	0.003	-	Chakraborty et al. (2016)
Sea bass (*Dicentrarchus labrax*)	1.0	1.58	9.30	1.81	0.61	0.94	0.94	0.2	Kocatepe and Turan (2012)

Vitamin E improved antibody responses after injection with hepatitis-B virus surface antigen, pneumococcal polysaccharides or tetanus toxoid (Goldrosen and Straus, 2004).

2.3. Minerals

2.3.1. Iron

Tuna, haddock, mackerel, sardines, cat fishes, oysters, mussels, clams, etc. are rich in iron content (Table 5). The required daily dietary allowance of minerals for different age group people is provided in Table 2. Iron plays essential role for the trasportation of oxygen throughout the body within haemoglobin complex. Heam iron found in aqua foods is readily bioavailable than non-heam plant sources. It is very important for growth, healing, energy production within cells, and DNA synthesis. Consumption of iron rich aqua-food improves the immunity function and is able to kill microbes (Ahmed et al., 2008). Iron is a critical factor for cell differentiation, cell growth, and immune response. It is essential for the synthesis of ribonucleotide reductase and DNA synthesis. It is also involved in regulation of cytokine production. Iron is important for differentiation and prolifertation T cells. It also helps to maintain the ratio between T helper cells and cytotoxic T cells. Iron deficiency decreases T-cell proliferation, differentiation, response, and the production of cytokines, for example IL-2. Iron supplementation has a positive effect on the levels of cytokine IL-6 in serum. In innate immunity, iron improves the function of macrophage and fight against microbial infections. It has been shown that the iron deficiency in children decrease phagocytic activity and antibody production. Iron supplemtation has shown noteworthy positive effect on iron level in anemia patients affected by malaria (Berger et al., 2000). The level of iron in body helps to fight against infectious diseases caused by bacteria, fungi, protozoa, and virus.

2.3.2. Iodine

The iodine content is high in seafoods, though the freshwater fishes also contain in low amount. Seafood is considered as a healthy diet which improves iodine intake status. Fishes such as cod, seabass, tuna, bele, baim, gojar, tengra, seaweeds, and other seafood like shrimp, scallops, and lobster are rich in iodine content (Table 5). Idone acts as fuel to maintain metabolic activity in the body. Iodine is mainly ingested either in organic or inorganic form, however the absorption of idone takes place in intestine as inorganic iodide. Iodine is mainly stored in thyroid in the form of iodinated amino acids and found in all extra cellular fluid. Idone is important for inducing the production of thyroid hormone which influences normal growth, metabolism, and oxygen consumption of cells and development of central nervous system. It has many non endocrinal functions such as it increases the movement of granulocytes into the areas of inflammation, increases IgG production in human lymphocytes and ultimately improves human immune functions. Iodine also improves the process of phagocytosis by granulocytes to kill microorganisms (Venturi and Venturi, 2009).

2.3.3. Magnesium

Many marine and freshwater fishes are rich in magnesium content like salmon, mackerel, halibut, shrimp, punti, mola, phasa and so on (Table 5). In living organisms, it is abundant in eukaryotic cells as a divalent cation. It is important for the survivability, development, and proliferation of immune cells. It helps to bind antigen in macrophage, regulate lymphocyte activation, apoptosis, and antibody dependent cytolysis (Arshad et al., 2020). Magnesium reduces the oxidative damages of DNA in mature lymphocytes. Magnesium is a co-factor which maintains the metabolism, structure of nucleic acids, and involves in DNA repair and replication (Petrović et al., 2016). Magnesium deficiency reduces the numbers of monocytes and NK cell functions. Magnesium deficiency also increases the production of cytokine IL-6, increase inflammation, and decrease T-cell ratios (Laires and Monteiro, 2008). Intaking magnesium was recommended for enhancing immunity against viral infections like COVID-19 (Jayawardena et al., 2020).

2.3.4. Selenium

Aquafoods such as tuna, sardines, clams, halibut, ilish, baim, kholisha, bele, rui, catla, shrimp, etc. are rich source of selenium (Table 5). Selenium helps to reduce the oxidative stress and inflammation of the body and enhances immune functions. Selenium is essential for the

Table 3. Recommended daily dietary allowance of different vitamins and minerals for different age group people.

Vitamins/Minerals	Recommended Dietary allowance					References
	Children 1 (4–8 years) M/F	Children 2 (9–13 years) M/F	Children 3 (14–18 years) M/F	Adults (19–50 years) M/F	Old age (51 to >70 years) M/F	
Vitamin A (μg/day)	400	600	900/700	900/700	900/700	Del Valle et al. (2011)
Vitamin B_1 (mg/day)	0.7	0.9/0.8	1.0/0.9	1.3/1.0	1.2/1.0	Strohm et al. (2016)
Vitamin B_2 (mg/day)	0.8	1.0/0.9	1.1/1.0	1.4/1.1	1.3/1.0	Strohm et al. (2016)
Vitamin B_3 (mg/day)	9.0	11.0/10.0	13.0/11.0	15.0/11.0	14.0/11.0	Strohm et al. (2016)
Vitamin B5 (mg/day)	2.0	3.0	4.0	5.0	-	Coates et al. (2010)
Vitamin B_6 (mg/day)	0.6	1.0	1.3/1.2	1.3	1.7/1.5	Coates et al. (2010)
Vitamin B9 (μg/day)	200	300	400	300–400	400	Del Valle et al. (2011)
Vitamin B12 (μg/day)	1.2	1.8	2.4	2.4	2.4	Del Valle et al. (2011)
Vitamin C (mg/day)	25	45	75	75	-	Coates et al. (2010)
Vitamins D3 (μg/day)	15.0	15.0	15.0	15.0	15–20	Del Valle et al. (2011)
Vitamin E (mg/day)	17.0	11.0	15.0	15.0	15.0	Del Valle et al. (2011)
Vitamin K (μg/day)	30.0	55.0	60.0	75.0	120.0/90.0	Coates et al. (2010)
Fe (mg/day)	10.0	8.0	10.0/15.0	8.0/18.0	8.0	Del Valle et al. (2011)
I (μg/day)	90.0	90.0	120.0/120.0	150.0/150.0	150.0/150.0	Del Valle et al. (2011)
Mg (mg/day)	130.0	240	410.0/360.0	400.0–420.0/310.0–320.0	420.0/320.0	Del Valle et al. (2011)
Se (μg/day)	30.0	40.0	55.0	55.0	-	Del Valle et al. (2011)
Ca (mg/day)	600.0	1000.0	1500.0	1450.0	-	Coates et al. (2010)
K (mg/day)	600.0	1000.0	1500.0	1450.0	-	Coates et al. (2010)
Zn (mg/day)	5.0	8.0	11.0/9.0	11.0/8.0	11.0/8.0	Del Valle et al. (2011)

Note: M = Male, F=Female.

function of selenoproteins which is cellular antioxidants, redox regulator, and counteracts reactive oxygen species. This protein is also important to regulate leukocyte and NK cell functions and maintains host defense system (Saeed et al., 2016). Selenium deficiency causes suppression of immune functions, impaired humoral and cell-mediated immunity. Suppression of immune function increases the incidence of cancer, cardiomyopathy, viral virulence, and decrease response to vaccination (Maggini et al., 2018). It enhances the differentiation and proliferation of T cells, and increases the number of T helper cells (Saeed et al., 2016). Selenium helps to maintain antibody levels of the body. In children, selenium deficiency increases the risk of respiratory tract infection in the first 6 weeks of life. Supplementation of selenium enhances immune response to viruses in selenium deficient individuals. Jayawardena et al. (2020) suggested to intake dietary selenium for immunity enhancement against viral disease like COVID-19.

2.3.5. Calcium, potassium, and phosphorus

Aquafoods are rich source of calcium (Table 5) and fish, crustaceans, and mollusks contain higher calcium content than terrestrial meats (Tacon and Metian, 2013). Salmon, sardine, cod fish bones, and shrimp are a good source of absorbable calcium. Halibut, tuna, cod, and snappers are good source of potassium. Carp, sardines, pollock, clam, etc. are rich in phosphorus content. Calcium is important for bone formation and plays vital role in maintaining muscle function. It is essential for metabolism and intracellular signaling. Intracellular calcium regulates many immune functions such as cell proliferation, cytokine production, and cytokine receptor expression. Calcium and phosphorus from fish and shellfishes are important for brain functions and strengthen body immune system. On the other hand, potassium is very important to control calcium concentration in cell and for signaling immune cells. It has been reported that 95% of COVID-19 patient had potassium deficiency and after potassium supplementation the patient responded well (Chen et al., 2020).

2.3.6. Zinc

Shellfishes such as oyster, clams, mussels, crabs, oysters, etc. are a potential source of zinc. Zinc is also available in fishes like salmon, sardines, flounder, shole, etc (Table 5). It assists the immune system to fight against invaded bacteria and viruses. The protein synthesis, DNA, and genetic material formulations in cellular level require optimum zinc level. Zinc supports the immune system working properly and wounds healing (Childs et al., 2019; Maggini et al., 2018). Around 30 % of the World's populations suffer from zinc deficiency and inadequacy which cause death of 8,00,000 people annually (Caulfield and Black, 2004). In developing countries, zinc deficiency is predominant and regardedas the fifth important risk factor for diarrhoeal and pneuminial diseases. Zinc also performs crucial roles in regulating homeostasis of immune process. The deficiency of zinc reduces Th1 cell number, decreased immunity including lymphocyte proliferation, production of IL-2, delayed-type hypersensitivity response, and antigen response. Additionally, cell activity, certain functions of neutrophils, and phagocytic activities of macrophage are destroyed due to zinc deficiency. On the other hand, supplementation of zinc can reverse the impairment in immune system and decrease deaths by infectious diseases. Zn protects the body from the ROS and RNS (Wu et al., 2019). It regulates the skin and mucosal membrane integrity, modulating cytokine release, and induces the proliferation of CD8+ T cells (Şanlier et al., 2019). Zinc aids in binding tyrosine kinase to T cell receptors in intracellular level which is a prerequisite for T lymphocyte growth and activation. Zinc also displayed to inhibit pro-inflammatory Th9 and Th17 cell differentiation and induce the growth of Treg cell population. It also supports Th1 response. In the healthy older people (>90 y), the quantity of NK cells were found strongly correlated with the blood zinc concentration (Ravaglia et al., 2000). Mocchegiani et al. (2008) reported the increment of NK cell cytotoxicity in both zinc deficiend and healthy elder (90) people due to zinc supplementation. Zinc has also been reported for the inhibition and treatment of viral colds (Goldrosen and Straus, 2004). The result has been shown that supplementation of zinc in malnourished children (3–24 months) of Bangladesh decreased the incidence of diarrhoea more than 50% (Roy et al., 1997). Zinc administration prohibited SARS coronavirus RNA-polymerase elongation and template bindling in Vero-E6 cells (Te Velthuis et al., 2010).

2.4. Fish oil and -3 polyunsaturated fatty acids

The principle dietary sources of ω-3 polyunsaturated fatty acids (ω-3 PUFAs) rich oil are seafoods (Table 6). Fatty fishes of temperate zone

Table 4. The contents and recommended daily dietary allowance of different vitamins available in aquafoods.

Species	A (mg/100g)	B1 (mg/100g)	B2 (mg/100g)	B3 (mg/100g)	B5 (mg/100g)	B6 (mg/100g)	B9 (mg/100g)	B12 (mg/100g)	C (mg/100g)	D3 (μg/100g)	E (mg/100g)	K (μg/100g)	References
African catfish (*Clarias gariepinus*)	18.1	0.07	0.03	1.13		0.08					0.34		Ersoy and Özeren (2009)
Fatty finfish	0.02–0.06	0.1–0.5	0.1–0.5	3.0–8.0	0.4–1.0	0.2–0.8	0.005–0.015	0.005–0.02		5–20	0.34		(Ariño et al., 2013)
Molluscs	0.01–0.1	0.05–0.3	0.05–0.3	0.2–2.0	0.1–0.5	0.05–0.2	0.02–0.05	0.001.0–0.05					
Crustaceans		0.02–0.3	0.02–0.3	0.5–3.0	0.5–1.0	0.1–0.3	0.001–0.01	0.001–0.01					
White finfish		0.05–0.5	0.05–0.5	0.1–5.0	0.1–0.5	0.15–0.5	0.005–0.015	0.001–0.005					
Cephalopods		0.05–0.5	0.05–0.5	1.0–5.0	0.5–1.0	0.3–0.1	0.01–0.02	0.002					
Horse mackerel	0.14	0.21	0.144	2.136		0.39							Erkan et al. (2010)
Rutilus frisii kutum	0.02	0.15		2.16						8.54			Hosseini et al. (2014)
Garden snail (*Helix aspersa*)	5.46	0.16	0.07	3.23		0.29					0.88		Çagiltay et al. (2011)
Sperata seenghala	0.168									1873.75	0.864	166.7	Lum et al. (2013)
Sea bass (*Dicentrarchus labrax*)		0.05	0.02	1.2	6.32		0.006		1.29		0.69		Kocatepe and Turan (2012)
Laminaria digitata	9.78	1.1	1.1	490.0		51.0		49.5	35.5		28.0		MacArtain et al. (2007)
Undaria pinnatifida	12.35	40.3	93.6	720.0		26.0	530.0	35.0			139.0		
Porphyra umbilicalis	6.8	7.7	27.4	76.1		12.7		76.9	161.0		11.0		
Spirulina platensis	84.0	44.0				0.3	0.04				1.2		Becker (2004)
Chlorella pyrenoidosa	48.0	1.0				2.3							
Puntius sophore	0.86										3.06	884.2	Mahanty et al. (2014)
Shrimp	0.002	0.05	0.03			0.13		0.002					Souci et al. (2000)
Mussels	0.054	0.16	0.22			0.76		0.008			0.75		
Cuttle fish	0.003	0.07	0.03	2.3		0.004					1.5	0.1	
Oyster	0.09	0.16	0.016			0.20	0.007	0.002			0.85	100.0	
Baim	0.03							0.002		1.3			Bogard et al. (2015)
										1.3			
Boro Kholisha	0.05							0.005		3.13	0.12		
Kachiki	0.08							0.003		1.5	0.09		
Koi	0.29									1.19			
Mola	2.50							0.007		2.03	0.27		
Tengra	0.01							0.003					

Table 5. The contents of different minerals (mg/100g) available in aquafoods.

Species	Fe	I	Mg	Se	Ca	K	Zn	References
African catfish (*Clarias gariepinus*)	1.2		18.4		400.1	181.7	0.35	Ersoy and Özeren (2009)
White finfish	0.2–0.6	0.02–0.1	15.0–30.0	0.02–0.1	10.0–50.0	200.0–500.0	0.2–1.0	Ariño et al. (2013)
Fatty finfish	1.0–5.0	0.02–0.1	20.0–50.0	0.02–0.1	10.0–200.0	200.0–500.0	0.2–1.0	
Crustaceans	0.2–2.0	0.05–0.1	20.0–200.0	0.05–0.1	20.0–200.0	100.0–500.0	1.0–5.0	
Molluscs	0.5–10.0	0.05–0.1	20.0–200.0	0.05–0.1	50.0–200.0	100.0–500.0	2.0–10.0	
Kutum roach (*Rutilus frisii kutum*)	0.88		21.15		13.78	406.79	0.31	Hosseini et al. (2014)
Garden snail (*Helix aspersa*)	0.52		17.05			105.40		Çagiltay et al. (2011)
Puntius sophore	11.5	126.0			974.82	228.3		Mahanty et al. (2014)
Cephalopods	0.2–1.0	0.02–0.1						Ariño et al. (2013)
Mullet *(Mugil cephalus)*	0.42		48.03	11.60	48.0	265.15	0.75	Kumaran et al. (2012)
Giant River-Catfish (Sperata seenghala)	4.51		129.0		458.11		2.94	Mohanty et al. (2012)
Labeo pangusia	5.97		56.6		9.7		3.75	Hei and Sarojnalini (2012)
Ompok bimaculatus	1.71		107.0		24.3		0.92	
Chlorella vulgaris	147.0		282.0		106.0		10.2	Yusof et al. (2011)
Callinectes pallidus	1.25		5724.14		3816.16	605.1	0.59	Elegbede and Fashina-Bombata, 2013
Cardisoma armatum	1.30		1404.08		1581.23	102.1	0.71	
Oysters (*Crassostrea madrasensis*)	3.37			0.01	168.1	270.1	3.56	Chakraborty et al. (2016)
Sea bass (*Dicentrarchus labrax*)	0.04	0.018	38.05	0.018	110.2	628.7	0.084	Kocatepe and Turan (2012)
Shrimp	6.1	0.1	67.0	0.1	92.0	230.0	2.2	Souci et al. (2000)
Lobster	1.0	0.1	24.0	0.1	61.0	220.0	1.6	
Mussels	4.2	0.1	30.0	0.1	24.0		1.8	
Cuttlefish	8.7	0.07		0.07	27.0	273.0	0.7	
Oyster	3.3	0.03	32.0	0.03	82.0		22.0	
Tiger shrimp	2.1	0.04	58.5	0.04			1.4	Dayal et al. (2013)
Baim	1.9	12.0	35.0	12.0	449.0	322.0	1.1	Bogard et al. (2015)
Boro Kholisha	4.1	0.1	44.0	2.3	1700.0	210.0	2.3	
Chapila	7.6	0.013	0.041	0.013	1063	281.0	2.1	
Magur	1.2	0.022	26.0	0.022	59.0	350.0	0.74	
Mola	5.7	0.017	49.0		853.0	152.0	3.2	
Shing	2.2	-	37.0	0.031	60.0	300.0	1.1	
Tengra	4.0	0.028	36.0	0.024	1093.0	203.0	3.1	

such as tuna, mackerel, salmon, herring, sardines, anchovies, etc. have been recognized as a balanced source of ω-3 PUFAs especially docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), and alpha-linolenic acid (Himaya and Kim, 2015). Omega-3 PUFAs are well known to immense contribution for cardiovascular protective functions. The other possible effects of ω-3 PUFAs are antiarrhythmic functions, modulation of autonomic functions, anti-inflammatory effects, reduce platelet aggregation, reduce blood pressure, vasodilation, plaque stabilization, and reduce triglyceride levels in bloods (Haq et al., 2018; Haq et al., 2020). It is recommended that patients with coronary heart problems should consume at least 1 g/day long chain ω-3 PUFAs from oily fish or as fish oil supplements and individuals without coronary heart problems should consume at least 250–500 mg/day.

As macronutrients, fish lipid and PUFAs not only provide energy but also regulate crucial cell functions. The ω-3 PUFAs derived from seafoods are known to contribute immune cell functions. The results have been shown that ω-3 PUFAs modulate both the innate and the adaptive immunity (Calder, 2017). The potent anti-inflammatory functions of ω-3 PUFAs include their capacity to hinder the formation of inflammatory mediators such as pro-inflammatory cytokines (IL-1b, TNF-α, IL-6), eicosanoids (PGE2, leukotrienes), chemokines (IL-8, MCP-1), platelet activating factors, adhesion molecules (ICAM-1, VACM-1, selectins), ROS, and RNS (Goldrosen and Straus, 2004). Omega-3 PUFAs not only inhibit pro-inflammatory mediators but also raise the formation of anti-inflammatory cytikine (IL-10). Omega-3 PUFAs perform anti-inflammatory activity by modulating gene activity. It also inhibits nuclear factor kappa-light-chain-enhancer of activated B cells (NF-kB) signaling. Dietary ω-3 PUFAs from salmon fish has significant effect on decreasing inflammation in obesy human. Fish oil supplementation increased IL-10 production in lactating women and improved abundance of probiotic microbiota *Lactobacillus* spp. and *Bifidobacterium* in their infants. The potent anti-inflammatory and protective effects of ω-3 PUFAs are found in patients with some chronic inflammation such as asthma, Crohn's disease, inflammatory bowel disease (IBD), ulcerative colitis, and autoimmune disorders like rheumatoid arthritis (Goldrosen and Straus, 2004). Supplementation of aquafoods rich in ω-3 PUFAs has recently been emerged as a food supplement and pharmaceutical applications (Haq et al., 2021). Therefore, it thas been suggested that ω-3 PUFAs are important for the immune modulation and protective factor against the development of future diseases.

2.5. Marine probiotics and fermented aquafoods

Various microbial species such as, *Bacteroides, Eubacterium, Prevotella, Clostridium, Lactobacillus, Bifidobacterium, Staphylococcus, Streptococcus, Enterococcus, Escherichia, Enterobacter,* etc could be both beneficial as well as harmful for the host body. The live beneficial microorganisms restricting the growth of harmful disease causing bacteria are referred as probiotic bacteria. The probiotics and prebiotics as nutraceutical and functional foods are popularly applied to improve body immunity. There are some strains of *Lactobacillus spp.* originated from the marine source have demonstrated unique probiotic characteristics. It is revealed that marine-derived *Lactobacillus spp.* has shown more advanced health benefits over terrestrial origin as probiotics. The immune response of probiotic is modulated in the gut through their interaction with intestinal epithelial cells, dendritic cells, and Peyer's patches (Baba et al., 2009). Probiotics exhibit positive impacts on immune system, stimulate innate and humoral immunity, prevent infection of influenza, and enhance influenza vaccine

Table 6. The contents and recommended daily dietary allowance of ω-3 polyunsaturated fatty acids and astaxanthin pigments available in aquafoods.

Omega-3 PUFAs	*Recommended Dietary Allowance*		
	600–1000 mg/day (Simopoulos et al., 2000).		
	Species	Quantity (% of total fatty acids)	References
	Kutum roach (*Rutilus frisii kutum*)	21.62)	Hosseini et al. (2014)
	Garden snail (*Helix aspersa*)	7.92	Çagiltay et al. (2011)
	Rainbow trout (*Oncorhynchus mykiss*)	17.46	Nurhan (2007)
	Sturgeon (*Huso huso*)	17.48	Li et al. (2007)
	Commerson's anchovy (*Stolephorus commersonii*)	18.87	Sankar et al. (2013)
	Mullet (*Mugil cephalus*)	21.83	Kumaran et al. (2012)
	Codium fragile	27.77	Ortiz et al. (2009)
	Gracilaria chilensis	2.98	
	Macrocystis pyrifera	5.92	
	Giant River-Catfish Sperata seenghala	20.01	Mohanty et al. (2012)
	Farmed Atlantic salmon (*Salmo salar L.*)	20.10	Jensen et al. (2012)
	Rainbow trout (*Oncorhynchus mykiss*)	22.92	Chávez-Mendoza et al. (2014)
	Seaweeds (*Laminaria sp.*)	17.44	Dawczynski et al. (2007)
	Chlorella vulgaris	0.46	Lum et al. (2013)
	Puntius sophore	9.65	Mohanty (2014)
	Oysters (*Crassostrea madrasensis*)	24.3	Chakraborty et al. (2016)
	Sea bass (*Dicentrarchus labrax*)	17.33	Kocatepe and Turan (2012)
	Pseudotolithus typus	28.8	Njinkoue et al. (2016)
	Atlantic salmon frame bone	13.35	Haq et al. (2017)
	Pseudotolithus elongatus	22.9	Njinkoue et al. (2016)
Astaxanthin	*Recommended dietary Allowance*		
	40–100 mg/day (Haq et al., 2018)		
	Species	Quantity	References
	Atlantic salmon (*Salmo salar*) frame bone	21.81 μg/g oil	Haq et al. (2018)
	Red porgy (*Pagrus pagrus*)	43.7–68.8 mg kg−1	Tejera et al. (2007)
	Atlantic salmon (*Salmo salar*)	3.5 mg kg−1	Yagiz et al. (2010)
	Brazilian redspotted shrimp waste (*Farfantepenaeus paulensis*)	0.7 μg/g waste, d.w.b.)	Sánchez-Camargo et al. (2011)
	P. semisulcatus	16.2 mg kg−1	Yanar et al. (2004)
	M. monoceros	18.0 mg kg−1	
	Atlantic krill (*Euphausia superba*)	11 mg/100g oil	Ali-Nehari et al. (2012)

immunogenicity. Probiotics induced the production of pro-inflmmatory cytokines to assist immune function against infection. Cytokine production depends on consumption of probiotic strains. *B. lactis* HN019 induces Interferon-α (IFN-α) production and consumption of *Lactobacillus rhamnosus* GG reduces TNF-α production (Kekkonen et al., 2008).

Fermentation of aquafoods improves digestibility and nutritional status as the substrate contains plenty of proteins and amino acids, vitamins, minerals, and essential fatty acids. Fermented foods demonstrated health functional effects by reducing blood cholesterol level, promoting immunity, protecting from pathogens, fighting against osteoporosis, carcinogenesis, allergies, diabetes, obesity, and atherosclerosis (Suraiya et al., 2018). Thongthai and Gildberg (2005) reported that the peptides recovered from Thai anchovy fish sauce stimulated the proliferation of human white blood cells. Substantial amount of co-enzyme Q10 (291 mg/g) has been reported in a fermented fish product from Korea (Pyo and Oh, 2011). Co-enzyme Q10 is an indispensable co-factor responsible for immune system enhancer, energy producer in cell, and powerful antioxidant. Fermented brown seaweed (*Sargassium thunbergii*) produced with a kimchi-derived bacteria has been applied as a prospective nutraceutical to counter inflammation (Mun et al., 2017). *Saccharina japonica* (Phaeophyceae) fermented with *Monascus* spp. exhibited adequate immunomodulatory and anti-inflammatory activity (Suraiya et al., 2019).

2.6. Carotenoids

Various carotenoid pigments are found in fish (salmon, rainbow trout, red snapper), shellfish (shrimp, lobster, crab, and crawfish), and seaweeds. In photosynthetic marine organisms, carotenoids perform as light energy harvester. Carotenoids act as antioxidants due to their complex ring structure which are able to inactivate harmful reactive oxygen species (Guerin et al., 2003; Lesser, 2006). Animals are unable to synthesize carotenoids; they deposit these from the plants they eat. There are various types of carotenoids such as astaxanthin, fucoxanthin, cantaxanthin, carotene, lycopene, lutein, violaxanthin, and zeaxanthin with pharmaceutical potential (Plaza et al., 2009; Jaswir et al., 2011). The red pigment astaxanthin is mainly found in oil of salmon, trout, shrimp, lobster, etc (Table 5). Astaxanthin is used as food coloring and nutraceutical agent. Fucoxanthin is mainly found in edible seaweeds which inhibit intestinal lipase activity and reduce obesity (Matsumoto et al., 2010). Carotenoids prevent oxidative stress, control the function of monocyte, central nervous system, and enhance body immunity (Hughes et al., 2000; London, 2010). Carotenoids reduce chronic inflammation and fight against cancer, eye disorders, rheumatoid arthritis, cardiovascular disease, and several neuro degenerative diseases (Abe et al., 2007; Vilchez et al., 2011).

2.7. Bioactive phenolic and flavonoid compounds

Freshwater edible aquatic weeds such as *Ipomoea aquatica* (Kolmi), *Nymphae arubra* (Red water lily, Lalshapla), *Nelum bonucifera* (Lotus), *Nymphaea nouchali* (Sadashapla) and *Alternanthera philoxeroides* (malancha) are rich in phenolic and flavonoid contents (Parimala and Shoba, 2013; Daffodil and Mohan, 2014; Yang et al., 2014). Seaweed also contains many bioactive compounds such as phenolics, flavonoids, vitamins, minerals, and other metabolites with potential health benefits (Athukorala et al., 2006; Ścieszka and Klewicka, 2019; Suraiya et al., 2018). Edible algae have been used as anti-inflammatory, anti-ulcerogenic, anti-microbial, and as nutritional supplement for hundred of years. Seaweed rich in flavonoids and phenolics has been demonstrated different functions such as antioxidant, anti-obesity, anti-inflammatory, and immunomodulatory properties (Bahar et al., 2016; Suraiya et al., 2019). Brown seaweed *Spatoglossum schroederi* extract considerably increase the gene expression of anti-inflammatory cytokine IL-10. Different metabolites from various algae exhibited antiviral, anticancer, and immunomodulatory activities. Fermentation process also increases the bioactive compounds/metabolites in fermented seaweed (Chen et al., 2019). Brown seaweed *Eisenia bicyclis* femented by yeast *Candida utilis* showed higher polyphenolics content and antioxidant activities (Eom et al., 2013). Brown seaweed, *Saccharina japonica* (formerly *Laminaria japonica)* fermented by *Aspergillus oryzae* showed the improvement of phenolic, flavonoids, and antioxidant activity. Fermentation process enriches the levels of phenolic, flavonoid, and other bioactive compounds of *Monascus* spp.-fermented brown seaweeds (Bae and Kim, 2010; Suraiya et al., 2018, 2019). However, the content of bioactive phenolic and flavonoid compounds have been found to be higher in fermented seaweeds compared with non-fermented one. Zhang et al., 2019 found a new natural phlorotannin (eckol) derived from marine brown algae that stimulated the mononuclear phagocytic system, activated dendritic cells, promoted the tumor-specific Th1 responses, increased the CD4+/CD8+ T lymphocyte ratio, and enhanced cytotoxic T lymphocyte responses. It showed potent stimulatory property on innate and adaptive immune responses.

Freshwater edible aquatic weed, *Alternanthera philoxeroides* rich in phenolics and flavonoids traditionally used in viral diseases, influenza, and as an immunomodulator (Hundiwale et al., 2012). Lotus, *Nelumbo nucifera* seeds retain varities of glycoproteins and other bioactive compounds showed wide range of biological activities such as activate human T cells, B cells, NK cells, enhance immunity and induced complement, cytokine secretion, and macrophage response (Yen et al., 2005). Thus, lotus seed extract also increase the number of leukocytes and lymphocytes, and significantly reduce the number of nutrophils. Extract of *I. aquatic* leaves demonstrated potent anti-inflammatory activity (Manvar and Desai, 2013). In addition, the seed extract of *N. nucifera* inhibited the production of pro-inflammatory cytokine TNF-α and increased the production of cytokine IL-10 (Mehta et al., 2013). The roots of *Ipomoea* contain different bioactive compounds which restrain HIV replication (Meira et al., 2012).

2.8. Functional carbohydrates (oligosaccharides and polysaccharides) from aqufood

Seaweeds are a good source of different types of bioactive polysaccharides. Exoskeleton of crustaceans and other arthropods such as shell of shrimp, lobsters, and crab etc. are also rich in different types of polysaccharides such as chitin, chitosan, and glucosamine. These compounds have shown different bioactivities against oxidative stress, aging, obesity, asthma, inflammation, diabetes, hypertension, cancer, and microbial infection. Chitosan activates macrophages to release cytokines and stimulates removal of cancer cells. Hydrolysis of chitin obtained form crustacean exoskeleton produces *N*-acetylglucosamine and glucosamine which exhibited anti-inflammatory activity (Himaya and Kim, 2015). Seaweed polysaccharides such as glucan, caragenan, laminarin, and sulfated polysaccharides show a wide range of activities such as antioxidant, antibacterial, antiviral, antitumor, and anti-inflammatory (Ngo and Kim, 2013). Brown seaweed, *Saccharina japonica* retains high amount of polysaccharides which exhibit variety of pharmaceutical features like, antiviral, antioxidant, and anti-inflammatory properties (Islam et al., 2013; Fang et al., 2015). Agar, laminarin, fucoidan, and navicula from seaweeds have shown the capability to fight against viral infections (Elaya Perumal and Sundararaj, 2020). Galacton and carrageenan from red seaweed showed antiviral properties against pathogenic influenza virus, herpes simplex virus, human papillomavirus, human rhinovirus, HIV, dengue virus, and hepatitis virus. Alginate performed antiviral properties against influenza A, hepatitis B, and HIV. Fucan from seaweeds fight against herpes simplex, sindbis virus, and human cytomegalo virus (Elaya Perumal and Sundararaj, 2020; Sansone et al., 2020). Navicula extracted from diatom showed double effect such as antiviral and anticancer effect, inhibit cancer cell proliferation by activating interferon signaling pathways. Polysaccharides from *N. rubra* have shown immune stimulating effect (Cheng et al., 2012). It has been shown that polysaccharides from red microalga *Porphyra* exhibited strong immunomodulatory activity by NF-κB-dependent immunocyte maturation and differentiation (Fu et al., 2019).

2.9. Marine invertebrates

Marine invertebrates such as molluscs, sponges, crustaceans, and echinoderms are good sources of bioactive peptides, phenols, steroids, alkaloids, terpenoids, strigolactones, and ether. Marine bivalves are rich in different types of compounds like alkaloids, terpenoids, steroids, polysaccharides, and peptides, etc. which have potential antiviral potency. Extracts or compounds isolated from different types of marine invertebrates possess anticancer, anti-helmintic, antihypertensive, antifungal, antiviral, antibacterial, and immune modulatory properties (Odeleye et al., 2020; Suleria et al., 2015). Marine mussels from *Mytilidae* family contain different bioactive compounds such as protein, lipid, carbohydrate, PUFAs, and iodine which show antimicrobial and anti-inflammatory activity. The extract of molluscs shows antioxidant, anticancer, anti-infectious, and cardiovascular protection properties. A wide range bioactive compounds were isolated from wide range of marine invertebrates, including shrimp, crab, cuttlefish, sea cucumber, and lobster which possess many health benefits. Various high valued medicines like cryotin enzyme (cancer inhibition) isolated from shrimp, neutrase (antioxidant) from sea urchin, protamex (cancer inhibition) from snow crab, neutraceutical supplements, and cosmetics. For example, pseudopterosin from the Caribbean sea whip prevented skin irritation (Odeleye et al., 2019). A peptide rich sea cucumber protein hydrolyzate found to demonstrate not only the reduction of ROS accumulation in cells but also directly scavenge free radicals (Guo et al., 2020).

2.10. Microalgae

Algae have been survived in the world for several millions of years and have faced many critical conditions. To survive in the adverse conditions, they developed different type of metabolites. The metabolites of the algae show antiviral activities and fight against different diseases. The microalgae are rich in amino acids, saccharides, vitamins, minerals, and many metabolites which facilitate the improvement of immunity power. The algae of Cyanophyta member's possess antiviral activity. Blue-green algae spirulina (*Arthrospira platensis*) showed high antiviral activities. The clinical trials of 30 patients against viral infections with *Spirulina* showed potential results against viral infections (Yakoot and Salem, 2012; Liu et al., 2020). Marine microalgal polysaccharides, navicula from *Navicula directa* (Bacillariophyta), and other A1 and A2 from dinoflagellate *Margalefidinium polykrikoides* (formerly *Cochlodinium polykrikoides)* exihibited antiviral acitivities against HIV-1 and influenza virus type A (Sansone et al., 2020).

Microalgae *Chlorella* (Chlorophyta) rich in many nutrients has boosted human immune system and been used for the treatment of cancer. Hydrophilic extracts of *Chlorella* have been exhibited many physiological functions such as hypoglycemic effects, lessen hyperlipidemic condition, and eventually improved the immunity system. The green micro alga, *Haematococcus lacustris* (formerly *Haematococcus pluvialis*) contains high amount of astaxanthin which increase the production of immunoglobulins (IgA, IgG, and IgM) by stimulating T-helper (Th) cells (Raja and Hemaiswarya, 2010). It also increases the immune response by NK cells and decreases stress related inflammation. *Navicula directa* has demonstrated antiviral activity against Herpes Simplex Virus 1 (HSV-1), Herpes Simplex Virus 2 (HSV-2). *A. platensis* has showed potential antival activity against mumps, influenza, human immunodeficiency viruse (HIV), polio, and measles virus. *Nostoc flagelliforme* (Cyanobacteria) is effective against influenza A virus and herpes virus (Sansone et al., 2020).

3. Conclusion

Aquafood comprises a large cosmopolitan of different plants and animals with potential bioactive compounds. There is sufficient amount of biofunctional compounds in the aquafoods and recently, a considerable number of studies have been conducted to determine the physiological roles of various compounds available in aquafoods. Regular and balanced consumption of aquafoods safeguards recommended daily dietary allowance and provides the needs of human body. They provide immune boosting support to the immune cells and initiate effective and rapid response against pathogens and prevent chronic inflammation. Several observational and clinical trails showed that bioactives from aquafoods, e. g., fishes, crustaceans, molluscs, seaweeds, etc. are involved with immune modulation, reduce the risk of influenza, and recover respiratory syndrome. So, aquafoods and their valuble compounds are highly recommended for the patients with the above mentioned problems. However, most of the studies have focused on the effects of the biofunctional compounds rather than applying the raw and cooked aquafoods; therefore, the effects of aquafoods and as raw and cooked products and their detail mechanisms can be further studies.

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