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Omega 3 Fatty Acids' Effects on COVID-19

Omega 3 Yağ Asitlerinin COVID-19 Üzerine Etkileri

Memnune ŞENGÜL
Seda UFUK

Department of Food Engineering, Atatürk University, Faculty of Agriculture, Erzurum, Turkey

ABSTRACT

Recently, the novel coronavirus, which is called severe acute respiratory syndrome coronavirus 2, has been responsible for the highly rapid spread of COVID-19 disease, globally. Until now, 535 million people were affected and 6.3 million people died due to this outbreak throughout the World. Although the lethality of this disease is lower than the severe acute respiratory syndrome coronavirus and Middle East respiratory syndrome, severe complications of this disease are attributed to "cytokine storm" that is the reason for the severe lung damage. The cytokine storm causes systemic inflammation, acute respiratory distress syndrome, septic shock, stroke, multiple organ dysfunction, and death. As a result of these symptoms, there are pivotal studies about vaccination, drug, and medication to prevent severe complications and treat patients with COVID-19. Besides these studies, some research shows that nutrients are able to manage the cytokine storm such as many types of vitamins, trace elements, and omega 3 fatty acids. Omega 3 polyunsaturated fatty acids have specific roles in the inflammatory process. Omega 3 fatty acids have a role in the improvement of the inflammatory balance. They interact with viral infection in disparate stages such as viral entry and replication. This study highlights the roles of omega 3 polyunsaturated fatty acids in the prevention and treatment of the COVID-19. In addition, omega 3 fatty acids show anti-viral and anti-inflammatory effects on the severe acute respiratory syndrome coronavirus 2 and increase survival rates in patients infected with COVID-19.

Keywords: Anti-inflammatory, anti-viral, COVID-19, omega 3 FAs, SARS-CoV-2

ÖZ

Son zamanlarda, SARS-CoV-2 olarak adlandırılan yeni koronavirüs, COVID-19 hastalığının dünya çapında oldukça hızlı yayılmasının sebebidir. Bu salgın nedeniyle dünyada şimdiye kadar 535 milyon kişi etkilendi ve 6,3 milyon kişi hayatını kaybetti. Bu hastalığın öldürücülüğü SARS-CoV ve MERS'ten daha düşük olmasına rağmen, bu hastalığın ciddi komplikasyonları, akciğer hasarının nedeni olan "sitokin fırtınasına" bağlanmaktadır. Sitokin fırtınası, sistemik inflamasyona, akut solunum sıkıntısı sendromuna, septik şoka, inmeye, çoklu organ yetmezliğine ve nihayetinde ölüme neden olur. Bu semptomların sonucunda meydana gelen ciddi komplikasyonları önlemek ve COVID-19 hastalarını tedavi etmek için aşı ve ilaç tedavisine yönelik önemli çalışmalar bulunmaktadır. Bu çalışmaların yanı sıra bazı araştırmalar, besinlerin birçok vitamin türü, eser elementler ve Omega 3 yağ asitleri gibi sitokin fırtınasını yönetme yeteneğine sahip olduğunu göstermektedir. Omega 3 çoklu doymamış yağ asitleri, enflamatuvar süreçte kendine özgü rollere sahiptir. Omega 3 yağ asitleri enflamatuvar dengenin düzelmesinde rol oynar. Viral enfeksiyonda, viral giriş ve viral replikasyon gibi farklı aşamalarda etkileşime girerler. Bu makale, COVID-19'un önlenmesinde ve tedavisinde, Omega 3 çoklu doymamış yağ asitlerinin rollerini vurgulamaktadır. Ek olarak, Omega 3 yağ asitleri, SARS-CoV-2 üzerinde anti-viral ve anti-inflamatuar etkiler gösterir ve COVID-19 ile enfekte hastalarda hayatta kalma oranlarını artırır.

Anahtar Kelimeler: Anti-enflamatuvar, anti-viral, COVID-19, omega 3 FAs, SARS-CoV-2

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Sorumlu Yazar/Corresponding Author: Memnune ŞENGÜL
E-mail: memnune@atauni.edu.tr

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Introduction

In December 2019, the coronavirus illness was first identified in Wuhan which is the capital city of Hubei province in China. The outbreak was initially detected in the Huanan Seafood Wholesale Market due to viral pneumonia from an unknown source. It has rapidly spread across the globe, and The Chinese Health Organization reported to the World Health Organization (WHO) and then WHO declared that the reason for outbreak is caused by a different coronavirus in Wuhan, China, on January 9, 2020.

The first death due to new coronavirus was reported on January 11, 2020, by the Chinese media. The illness caused by the novel coronavirus was named COVID-19 by WHO on February 11, 2020. Subsequently, 26 different countries were rapidly affected by COVID-19 after China. Following that, WHO announced this disease as a pandemic in March 2020 (WHO, 2020). According to the latest data, internationally, the confirmed cases of COVID-19 are reported to be 535,248,141, and there have been 6,313,229 deaths until June 2022 (WHO, 2022). The mortality rate of COVID-19 is approximately 2%, and the rate of hospital mortality is roughly 10% (Weill et al., 2020).

The novel coronavirus (severe acute respiratory syndrome coronavirus 2 (SARS-CoV2)) symptoms displayed by the infected individuals are commonly fever, cough, headache, sore throat, shortness of breath, tiredness, and loss of smell or taste. In addition, there are less common symptoms shown by infected patients such as diarrhea, joint pain, stomachache, nausea, dizziness, and a decrease in blood pressure (Abdullah et al., 2021). Even though the novel SARS-CoV2 disease is symptomatic in infected people, some people who tested positive for the coronavirus may be symptomless. Patients may exhibit severe symptoms for a variety of reasons, including age, gender, obesity, smoking, and underlying health issues such as cancer, asthma, diabetes, and chronic medical conditions (Asher et al., 2021). These serious symptoms and complications may be dyspnea hypoxia, septic shock, and stroke, respiratory failure (acute respiratory distress syndrome (ARDS)), and multiorgan dysfunction (Asher et al., 2021).

For good health and disease prevention, omega 3 fatty acids (FAs), which are polyunsaturated fatty acids, are known to provide essential dietary nutrients (Surette, 2008). Omega 3 polyunsaturated FAs consist of, firstly, α-linolenic acid with 18 carbon atoms and 3 double bonds, secondly, eicosapentaenoic acid (EPA) with 20 carbon atoms and 5 double bonds, thirdly, docosapentaenoic acid with 22 carbon atoms and 5 double bonds, and finally, docosahexaenoic acid (DHA) with 22 carbon atoms and 6 double bonds. Omega 3 index (O3I) test is the measurement of the amount of the omega 3 FAs (EPA and DHA) in the red blood cell membranes, and it is used to show the ratio of total omega 3 FAs to all other FAs (Hathaway et al., 2020). Adequate intakes (AIs) of omega 3 FAs according to individuals' ages are demonstrated in Table 1.

Eicosapentaenoic acid and DHA are responsible for the synthesis of various inflammatory mediators including prostaglandins (PG), resolvins, leukotrienes (LT), protectins, maresins, and thromboxanes (TX). Long-chain omega 3 FAs have significant anti-inflammatory roles, and with these properties, they can help reduce morbidity and mortality due to infections (Asher et al., 2021). In this manner, these FAs can prevent the effects of inflammatory processes by means of their anti-inflammatory effects. Omega 3 FAs regulate different metabolic processes including visual and brain development, inflammatory reactions, stroke, and cellular functions in the body (Surette, 2008). Also, omega 3 polyunsaturated FAs have positive effects on depression as these FAs can be found in the nervous system of individuals. It has been found that individuals with a low intake of fish and omega 3 polyunsaturated FAs in their diet have a higher risk of depression (Eskici, 2020). According to recent study, omega 3 FAs and lipid emulsions affect the inflammatory process, in both ARDS and other severe conditions (García de Acilu et al., 2020). Omega 3 FAs may promote the ability of phagocytosis and enhance and activate the function of the macrophages. Moreover, omega 3 FAs (fish oil) can improve antiviral response by means of the innate immune system that hinders viral replication (Hathaway et al., 2020).

Table 1.
Adequate Intakes (AIs) of Omega 3 Fatty Acids (Institute of Medicine, 2005)

Age	Male	Female	Pregnancy	Lactation
0–1 year*	0.5 g	0.5 g		
1–3 years**	0.7 g	0.7 g		
4–8 years**	0.9 g	0.9 g		
9–13 years**	1.2 g	1.0 g		
14–50 years**	1.6 g	1.1 g	1.4 g	1.3 g
51 and above years**	1.6 g	1.1 g		

Note: *Total omega 3 fatty acids, **Apha-linolenic acid.

In the past, people ate food with a low caloric intake of fats and saturated FAs (Fatty acids) such as meat, fish, plants (vegetables), fruits like berries, and nuts. Therefore, the ratio of omega 6/omega 3 (1-2 : 1) was balanced, and it allowed for the development of humans' cognitive and cerebral properties. On the other hand, at present, this ratio of omega 6/omega 3 changes (20-30 : 1) due to a low intake of omega 3 and a high intake of omega 6 FAs. Another factor is the rise in the intake of trans-FAs which was negligible in the past (Candela et al., 2011). A low intake of EPA and DHA causes a rise in inflammatory processes and inappropriate fetal improvement, poor cardiovascular health, and also leads to an increased risk of the occurrence of Alzheimer's disease (Swanson et al., 2012).

Long-chain omega 3 polyunsaturated FAs, EPA and DHA, display anti-inflammatory roles that are able to decrease morbidity and mortality due to novel coronavirus disease. Serious COVID-19 symptoms and even death are related to fast elevations of inflammatory cytokines containing interleukin (IL)-1β, tumor necrosis factor-alpha, and IL-6. Due to this fast elevation of cytokines, cytokine storm (macrophage over activation syndrome) occurs. Long-chain omega 3 FAs may modulate the inflammatory responses and release of cytokines by decreasing cytokine release (Asher et al., 2021).

Some nutrients like vitamins, minerals, and FAs have noteworthy properties in the management of cytokine storms. For instance, omega 3 polyunsaturated FAs (EPA and DHA) can directly affect the immunological response (Szabó et al., 2020). The major reason for death in infected people due to COVID-19 is multi-organ dysfunction because of cytokine storms. To decrease pro-inflammatory cytokines, intake of omega 3 FAs may be increased because they can decline viral entry and provide a better immune system. Moreover, they can lessen the severe conditions of patients with COVID-19 disease (Hathaway et al., 2020). Supplementing omega-3 FAs to COVID-19 patients may help to reduce inflammation. Omega 3 FAs are able to play an important role to prevent cytokine storm by reducing the severity of inflammation and thus are able to decline the risk of mortality in patients infected with COVID-19 (Akram et al., 2021).

Recently, the COVID-19 outbreak has been rapid in the transmission from human to human globally. In addition to vaccination studies and vaccination procedures, alternative treatment methods should be provided for the patients who are at risk. For this purpose, omega 3 FAs, which are natural, accessible, safe, and inexpensive, can be used as an alternative treatment (Hathaway et al., 2020).

Coronavirus

Coronaviruses are a member of spherical virus family and consist of RNA and 4 structural proteins which are nucleocapsid protein, envelope protein, membrane, and spike glycoproteins (Haköksüz et al., 2020). These coronaviruses are enveloped, single-stranded, non-segmented RNA with linear positive-sense RNA viruses (Tang et al., 2020). The diameter of the coronavirus is 125 nm with its 3-dimensional structure and has a size change from 26 to 32 kbs in length (Hathaway et al., 2020; Shereen et al., 2020). Figure 1 shows the taxonomy of the coronavirus, and according to this figure, coronavirus is classified under the Riboviria realm, Nidovirales order, coronaviridae family, and orthocoronavirinae subfamily. Orthocoronavirinae subfamily has 4 different genera under its own which are alpha coronavirus, beta coronavirus, gamma coronavirus, and delta coronavirus (Aydoğdu et al., 2021). These coronaviruses, which are abundantly found in nature, generally infect some species such as rats, pigs, turkeys, etc.; however, alpha coronaviruses and beta coronaviruses (alpha coronaviruses 229E and NL63 and beta coronaviruses OC43, HKU1, SARS-CoV, MERS CoV and SARS-CoV2) affect individuals (Hathaway et al., 2020). In addition, Table 2 demonstrates a brief comparison of the SARS-CoV, MERS CoV, and SARS-CoV-2. There are some similarities between SARS-CoV and SARS-CoV-2. They belong to the same family called coronaviridae. Bats are their primary reservoir, and humans are their primary host . They use the same receptor, which is the angiotensin-converting enzyme 2 (ACE-2), to attach to the human body and enter respiratory cells. These coronaviruses are transmitted from human to human by means of respiratory droplets and contact with sick people. SARS-CoV and SARS-CoV-2 are included in the genus beta coronavirus (Haköksüz et al., 2020). The symptoms such as fever, shortness of breath, and cough are similar symptoms caused by COVID-19 and SARS-CoV. They can appear as ground-glass opacities according to x-ray imaging of the chest. To avoid these coronaviruses, it is crucial to keep a social distance while providing hand and respiratory hygiene (Hathaway et al., 2020).

The life cycle of SARS-Cov-2 can be explained by different steps in the host cells. Figure 2 illustrates the life cycle of SARS-CoV-2 in the host cell. Attachment of coronaviruses to the host cell is supported by spike proteins (S) of the viral particle. Also, spike proteins ease viral binding to the surface of cells (Hoffman et al., 2020). These spike proteins are able to bind to ACE-2, which is located on the human cell surface, as an entry receptor (Aryan et al., 2021). The S protein can be activated in the viral particle by the transmembrane serine protease 2 (TMPRSS2), the enzyme found near the receptor of ACE-2. A combination of S proteins and enzymes facilitates the viral entry to the cytoplasm of the host membrane. The virus can enter the host cell either via membrane

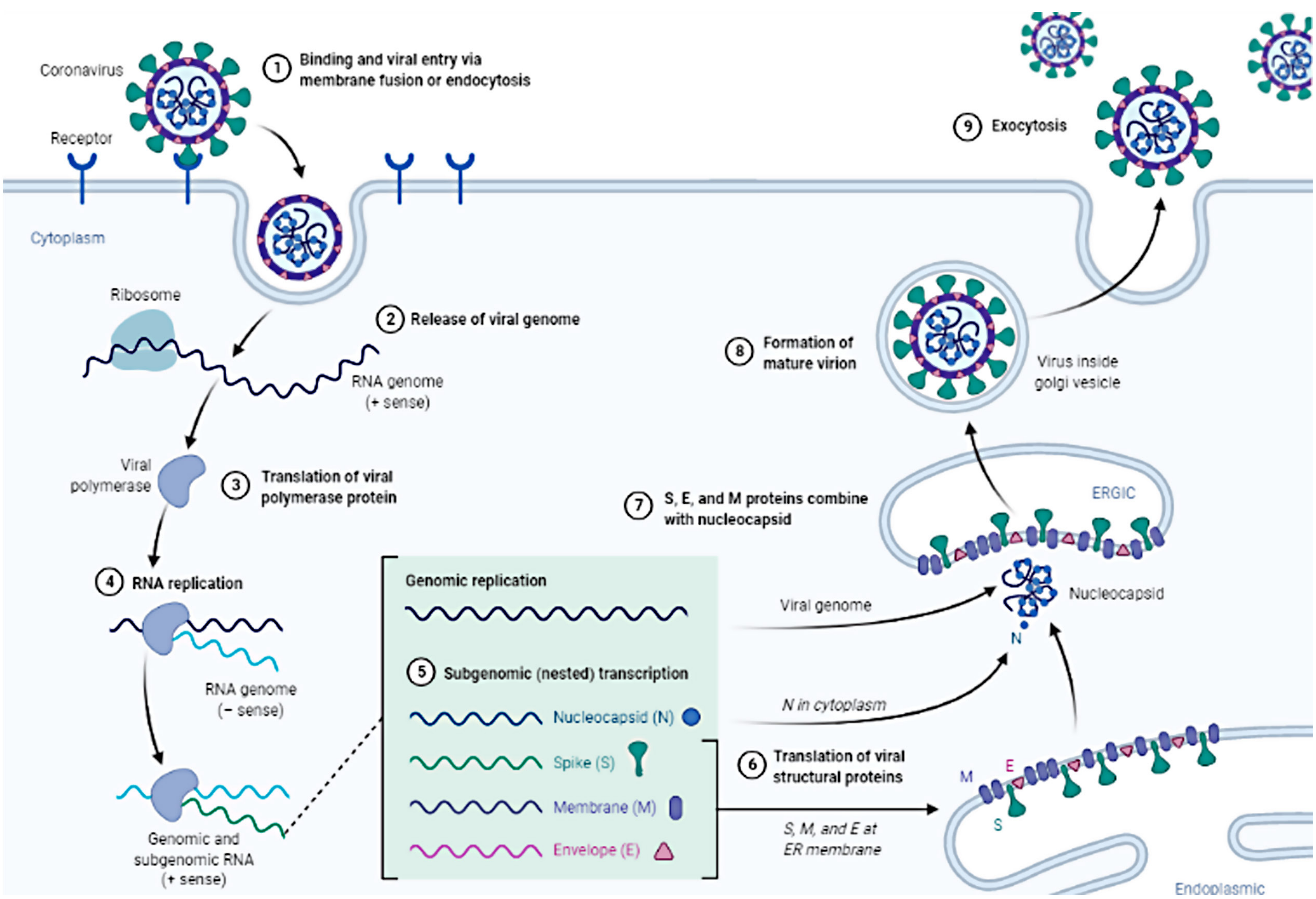

Figure 1.
Taxonomy of the Coronavirus and its Close Relatives (Tang et al., 2020).

Table 2.
Comparison of SARS-CoV, MERS-CoV, and SARS-CoV2 (Hathaway et al., 2020; Tang et al., 2020)

	SARS-CoV	MERS-CoV	SARS-CoV2
Family	Coronaviridae	Coronaviridae	Coronaviridae
Illness caused	SARS	MERS	COVID-19
Time of origin	November, 2002	June, 2012	December, 2019
First outbreak	Guangdong, China	Jeddah, Saudi Arabia	Wuhan, China
Spread	Animal to person, person to person	Animal to person, person to person	Animal to person, person to person
Transmission	Respiratory droplets, personal contact	Respiratory droplets, direct contact, aerosols	Respiratory droplets, direct contact, aerosols
Primary host	Human	Human	Human
Reservoir	Bats	Camels	Bats
Incubation time	5 days	5 days	2–14 days
Receptor	ACE-2	DPP4, CD26, and pneumocytes	ACE-2
Common symptoms	Cough, fever, malaise, headache, shortness of breath, diarrhea	Cough, diarrhea, fever, shortness of breath, acute respiratory distress syndrome	Cough, shortness of breath, fever, fatigue
Prevention	Social distancing, respiratory and hand hygiene	Hand washing after contacting animals, not drinking raw camel milk, and eating raw meats	Social distancing, respiratory and hand hygiene
Case fatality rate	9.6%	34.3%	1.38%-3.4%

Note: SARS-CoV2 = severe acute respiratory syndrome coronavirus 2; MERS = Middle East respiratory syndrome; ACE-2 = angiotensin-converting enzyme 2.

fusion or endocytosis. Subsequently, the virus can release positive-sense viral RNA in the cytoplasm of the host cell by means of uncoating. The viral polymerase proteins can be translated by the host ribosomes using the positive-sense RNA of the viral particle. After that, the positive-sense RNA replicates just as the negative-sense RNA. Subsequently, genomic replication and subgenomic transcription occur, and during these processes, there is more production of the positive-sense RNA by using negative-sense genome and mRNA for viral structural proteins which are envelope (E), spike (S), nucleocapsid (N), and membrane (M), independently. Then, the structural proteins (S, M, and E) in the endoplasmic reticulum membrane and nucleocapsid proteins in the cytoplasm are combined altogether. Eventually, the release of mature virus inside the golgi vesicle is completed via exocytosis from the infected cell (Hathaway et al., 2020). The released virus can infect other cells by the same process as mentioned.

The most important criterion for the transmission potential of infectious disease is the basic reproductive coefficient and is expressed as R0. A R0 for an infectious illness is known as a single numeric value. This value typically expressed as an outbreak is expected to continue if R0 is greater than 1.0 and to end if R0 has a value smaller than 1.0 (Delamater et al., 2019). For COVID-19, R0 is calculated between the range of 2.24 and 3.58 in China. Globally, to end the outbreak, the R0 value should be smaller than 1.0. Therefore, to decrease this value to smaller than 1.0, there are some interventions and precautions such as quarantine, isolation, social distance, and wearing medical mask (Ataç et al., 2020). R0 value for SARS-CoV-2 is greater than the R0 values of SARS-CoV (R0 is between 1.0 and 1.7) and MERS (R0 < 1.0) (Hathaway et al., 2020).

The most probable evidence is that SARS-CoV-2 is a zoonotic transmission from the animal marketplace in China, Wuhan. A considerable number of individuals were subjected to this marketplace. Therefore, this event suggests that the first transmission is from animal to human (Hathaway et al., 2020).

Coronavirus spreads from person to person due to close contact of people with infected patients who are exposed to sneezing, coughing, aerosols, and respiratory droplets. Aerosols can enter the human body through the nose, eyes, and mouth during inhalation (Shereen et al., 2020).

The coronavirus is able to thrive for a definite time outside of the host membrane and can persist for many hours or days on a large number of surfaces such as door handles, mobile phones, etc. Therefore, it facilitates the virus transmission from external surfaces to the host cell through contact with the nose, mouth, and eyes (Fiorillo et al., 2020; Hathaway et al., 2020).

Individuals of all ages are at risk to be affected by the novel coronavirus (COVID-19). Some infected people are more vulnerable to life-threatening infections. According to studies on SARS-CoV-2, the risk groups most severely affected by the disease are the older age group, especially those over 60, those with underlying chronic illnesses, and also patients with comorbidities such as cardiovascular disease, heart attack, stroke, chronic respiratory disease, cancer, and diabetes (Ataç et al., 2020). In addition, smokers are more susceptible to COVID-19 because they smoke with their fingers with contact with their lips and so the risk of transmitting virus from hand to mouth increases. Also, lung disease or shortness of breath increases the risk (Zabetakis et al., 2020).

The Relationship Between Omega 3 Fatty Acids and Health

The essential fatty acids (EFAs), which are required to be taken via dietary intake by individuals, were first investigated in 1963 by Arild Hansen and his colleagues. Subsequently, there is great scientific interest in EFAs and their roles in the human body. In addition, the discoveries and the researchers have developed day by day (Candela et al., 2011).

Fatty acids are pivotal to humankind due to their significant roles. Firstly, they are major energy sources. The latter shows the structural roles such as being part of the cell membrane. Finally, they have a role in cell signaling and giving a response, respectively

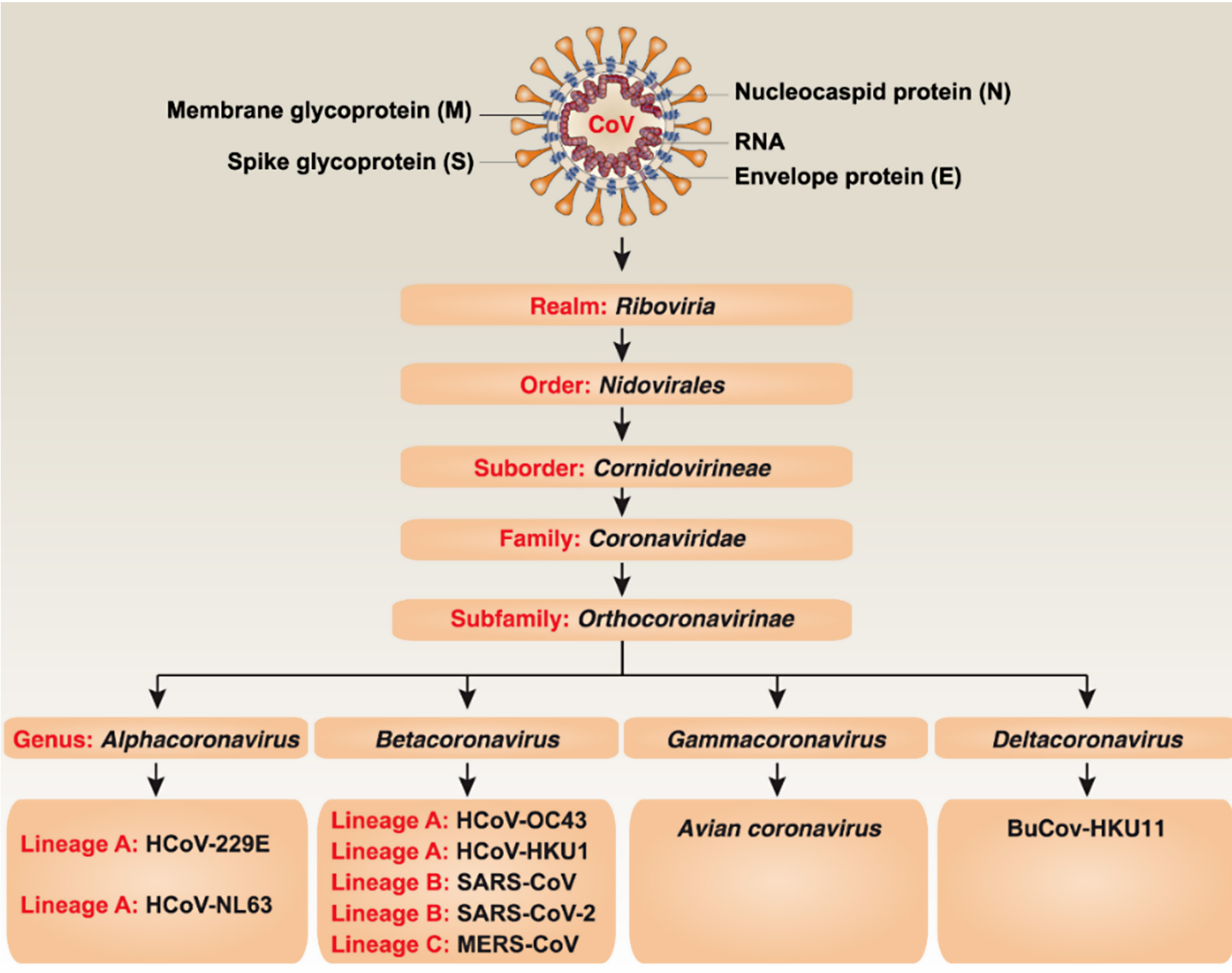

Figure 2.
Attaching, Viral Entry, and Replication Cycle of SARS-CoV-2 (Haköksüz et al., 2020). SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2.

(García de Acilu et al., 2015). Both the omega 6 and omega 3 EFA series are necessary for the growth and development of individuals and prevention of some types of diseases such as coronary diseases, diabetes, cancer, inflammatory illnesses, and also hypertension (Candela et al., 2011). In addition, omega 3 polyunsaturated FAs (EPA and DHA) are crucial for appropriate fetal development and aging (Swanson et al., 2012). Essential FAs are unsaturated FAs that are classified as linoleic acid [LA or 18:2(n-6)] and α-linolenic acid [ALA or 18:3 (omega 3) or 18:3 omega 3]. Essential FAs have to be obtained through the diet since individuals are not able to synthesize these FAs due to the lack of required enzymatic machinery (Surette, 2008). While the LA is the precursor of arachidonic acid, ALA is the metabolic precursor of both the eicosapentanoic acid (EPA, 20 : 5 ω3) and the docosahexanoic acid (DHA 22 : 6 ω3). Although individuals can convert ALA into EPA and DHA, the direct ingestion of the EPA and DHA via diet seems more efficient (Surette, 2008). The arachidonic acid, which transforms into eicosanoids by means of oxygenation and lipoxygenase enzymes, can be either obtained from the diet or can be converted from LA. The eicosanoids are TX, LT, and PG, and these eicosanoids have crucial inflammatory roles, and an increase in the synthesis AA leads to autoimmune diseases, cancer, cardiovascular disease, and inflammatory (Canbolat, 2016). On the other hand, EPA and DHA are precursors of a group of inflammati on-resolving mediators (IRM) which are resolvins, protectins, and Maresins. Inflammation-resolving mediators are responsible for resolving inflammation actively and also downregulating cytokine synthesis (Asher et al., 2021).

Omega 3 FAs have a significant role in the prevention of the development of the cancer types which are colon, liver, breast, and prostate cancers (Candela et al., 2011). Cancer is a severe disease and is caused by either epigenetic or genetic changes. Specifically, there is a variety of factors affecting the development of the cancers, such as hormonal alterations, mutation, smoking, consumption of alcohol, and pollution (Nabavi et al., 2015). Omega 3 polyunsaturated FAs can inhibit the initiation of cancer and cell cycle, increase the death of cells, and decrease inflammation. In addition, they are able to prevent angiogenesis and metastasis in either genetic or epigenetic ways; therefore, they stress that omega 3 FAs have anticancer roles in the human body (Jing et al., 2013).

The FAs have a crucial role in hindering viral infection. It is known that the FAs with more carbon chains have the maximum activity against viral infection (Aryan et al., 2021). Omega 3 long-chain polyunsaturated FAs (LC-PUFA) may have disparate roles against viral infection that aids in the prevention of viral entry and also replication of the virus (Weill et al., 2020).

A study conducted by Asher et al. (2021) showed the relationship between COVID-19 outcome and omega 3 FA levels. According to this study, omega 3 FAs provide active inflammatory mechanism and have beneficial effects on the treatment of COVID-19 infection by lowering cytokine levels. Therefore, when the cytokine level decreases, the cytokine storm, which can be the reason for the death of COVID-19, can be hindered.

In order to investigate the relationship between COVID-19 and omega 3 FAs, another study was conducted by Louca et al. (2021). They studied COVID-19 patients who had low O3I level. They took dietary supplements more than 3 times weekly for 3 months. As a result of this study, they found that using the omega-3 FA supplements decrease the risk by 12% of being infected with COVID-19 infection (Louca et al., 2021).

An alternative case–control study showed that there is a converse correlation between the O3I and the severity of COVID-19 infection. According to this study, the risk of hospitalization and main clinical symptoms of COVID-19 can reduce by high level O3I. In addition, consumption of fish or omega 3 supplements may dramatically minimize the socioeconomic and healthcare costs of severe COVID-19 (Ramírez-Santana et al., 2022).

According to Kagawa (2022), the production of protectin, which declines morbidity and mortality due to COVID-19 infection, is responsible for the anti-inflammatory activities of both EPA and DHA. Additionally, protectin prevents COVID-19 infection by promoting phagocytosis and neutrophil differentiation.

The main sources of omega 3 FAs in the diet are fresh fish including salmon, mackerel, herring, sardines, sturgeon, squid, trout, mussels, and sea bass. Moreover, some fish foods like microalgae and also other invertebrates contain a great amount of EPA and DHA. In addition, many microorganisms and microalgae are rich in EPA and DHA such as marine protists and dinoflagellates. Although the main sources of EPA and DHA are fresh fish and marine origin, there are non-marine foods that contain omega 3 FAs such as cereals, nuts, flaxseed, chia seed, soybean, some fruits, and vegetables (Hathaway et al., 2020). Minor sources of the omega 3 FAs are found in egg yolks, white meats, and also red meats. In addition, some edible mushrooms contain omega 3 FAs (Nabavi et al., 2015).

Table 3 shows the main food sources and their EPA and DHA density (mg/100 g food).

Table 3.
The Food Items with the Highest EPA and DHA Density (Kranz et al., 2015)

	Main Food Description	EPA and DHA Density (mg/100 g food)
1	Roe (sturgeon)	6548
2	Mackerel (baked-broiled)	2351
3	Sardines (skinless, boneless, water-packed)	2149
4	Herring (baked/broiled)	2024
5	Squid (dried)	1848
6	Mackerel (floured-breaded, fried)	1607
7	Salmon (canned)	1587
8	Sardines (tomato-based sauce-mixture)	1396
9	Herring (pickled)	1389
10	Salmon (baked-broiled)	1079
11	Salmon (cooked by NS cooking method)	1056
12	Salmon (steamed-poached)	1050
13	Trout (baked-broiled)	1009
14	Sardines (canned)	983
15	Sardines (cooked)	982
16	Mussels (steamed-poached)	875
17	Brains (cooked)	847
18	Salmon (floured-breaded, fried)	834
19	Trout (breaded-battered, baked)	765
20	Sea bass (steamed-poached)	741

Note: EPA = eicosapentaenoic acid; DHA = docosahexaenoic acid.

Eicosapentaenoic acid and DHA consumption is crucial to maintain important physiologic functions and these omega 3 FAs have significant roles in individuals' health. Intake of EPA+DHA can increase the level of O3I effectively but not ALA intake (Maki et al., 2019). A low level of O3I is related to some health issues such as cognitive function problems, depression, cardiovascular diseases, and other diseases. Normally, the intake of plant-origin omega 3 FA ALA can raise the quantity of EPA and DHA. Nevertheless, it is poor to convert ALA to EPA and DHA cannot be increased by ALA (Köhler et al., 2017). Bioavailability is the term that a target nutrient should be digested/absorbed and metabolized systematically through normal circulation, and also the bioavailability of nutrients can vary with different factors (Schönfeldt et al., 2016). The diet with FFAs has higher bioavailability than the diet containing ester. While DHA has high bioavailability due to a poor beta-oxidation substrate content, ALA has little bioavailability with a higher rate of oxidation (Hathaway et al., 2020).

It is recommended that the intake of omega 3 FAs (EPA+DHA), either supplemented or from its source, should be between 0.5 g and 1.8 g per day to prevent deaths and other problems related to heart diseases. American Heart Association (AHA) suggests the consumption of at least 2 times of fish in a week. The AHA recommends people with cardiovascular disease consume nearly 1 g of combined EPA and DHA cell daily and that people with hypertriglyceridemia consume 2-4 g of omega 3 FAs (EPA+DHA) to lower triglyceride levels (Kris-Etherton et al., 2003). In addition, another study indicated that daily 5 g of omega-3 FAs intake considerably reduces the levels of a variety of pro-inflammatory cytokines (Sears, 2018).

Conclusion

As shown in the study, there are different functions of omega 3 polyunsaturated FAs as a natural treatment and prevention of diseases. These omega 3 FAs show their effects by being embodied in the cell, afterward affecting the receptors to prevent signals for activation of the inflammatory response and finally help to heal symptoms of COVID-19. Omega 3 FAs (EPA and DHA) are the precursors of resolvins, which are responsible for reducing pro-inflammatory mediators and decreasing lung inflammation in the body. Besides their anti-inflammatory effects, omega 3 FAs have important roles in the body in preventing some serious diseases such as cardiovascular disease, osteoporosis, hypertension, type-II diabetes, asthma, and some types of cancers. In addition, omega 3 FAs are able to optimize visual signaling and brain and cognitive development. Moreover, omega 3 FAs are accessible, easy to use, inexpensive, and have natural nutrients. Owing to having positive effects, omega 3 FAs can be a good choice and worth studying during the pandemic duration. Therefore, more trials and studies on omega 3 FAs and supplements are required to understand in the future.

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References

Abdullah, N. K., Khalil, R., Qaddoura, D. K., & Alash, R. J., (2021). Survey study: COVID-19 symptoms and lifestyle. *World Journal of Biology Pharmacy and Health Sciences*, *5*(2), 33–44. [CrossRef]

Akram, Z., Allenki, A., Kishore, S., Ogwu, D., Titilayo Adefalu, O., Lisseth Valle Villatoro, A., Adebukola Omole, J., Uddin, G., Gopal, S., Mir Khan, A., Nuzhat Lodi, M., Shahbaz, T., Ul Huda Nabeel, N., Vega, L., Tariq, U., & B Nkongho, M. (2021) Role of OMEGA-3 fatty acid supplementation in COVID-19 patients: A narrative review. *Archives of Internal Medicine Research*, *4*(2), 177–183. [CrossRef]

Aryan, H., Saxena, A., & Tiwari, A. (2021). Correlation between bioactive lipids and novel coronavirus: Constructive role of biolipids in curbing infectivity by enveloped viruses, centralizing on EPA and DHA. *Systems Microbiology and Biomanufacturing*, *1*(2), 186–192. [CrossRef]

Asher, A., Tintle, N. L., Myers, M., Lockshon, L., Bacareza, H., & Harris, W. S. (2021). Blood omega-3 fatty acids and death from covid-19: A pilot study. *Prostaglandins, Leukotrienes, and Essential Fatty Acids*, *166*, 102250. [CrossRef]

Ataç, Ö., Uçar, A., & Taşdemir, M. (2020). COVID-19 Nedir; Epidemiyoloji, Kaynak ve Bulaş Yolları, Risk Grupları Nelerdir? In Ö Yiğit, (Ed.), *Kulak Burun Boğaz ve COVID*. Türkiye Klinikleri.

Aydoğdu, M. O., Altun, E., Chung, E., Ren, G., Homer-Vanniasinkam, S., Chen, B., & Edirisinghe, M. (2021). Surface interactions and viability of coronaviruses. *Journal of the Royal Society, Interface*, *18*(174), 20200798. [CrossRef]

Canbolat, E. (2016). Araşidonik asit metabolitlerinin oluşum mekanizması ve bazı hastalıklardaki rolü. *EJOVOC (Electronic Journal of Vocational Colleges)*, *5*(6), 20–29.

Candela, G. C., Lopez, L. M. B., & Kohen, V. L. (2011). Importance of a balanced omega6/omega3 ratio for the maintenance of health: Nutritional recommendations. *Nutricion Hospitalaria*, *26*, 323–329. [CrossRef]

Delamater, P. L., Street, E. J., Leslie, T. F., Yang, Y. T., & Jacobsen, K. H. (2019). Complexity of the basic reproduction number (r0). *Emerging Infectious Diseases*, *25*(1), 1–4. [CrossRef]

Eskici, G. (2020). Covid-19 pandemia: Nutrition recommendations for quarantine. *Anadolu Kliniği Tıp Bilimleri Dergisi*, *25*, 124–129. [CrossRef]

Fiorillo, L., Cervino, G., Matarese, M., D'Amico, C., Surace, G., Paduano, V., Fiorillo, M. T., Moschella, A., Bruna, A., Romano, G. L., Laudicella, R., Baldari, S., & Cicciù, M. (2020). Covid-19 surface persistence: A recent data summary and its importance for medical and dental settings. *International Journal of Environmental Research and Public Health*, *17*(9), 3132. [CrossRef]

García de Acilu, M., Leal, S., Caralt, B., Roca, O., Sabater, J., & Masclans, J. R. (2015). The role of omega-3 polyunsaturated fatty acids in the treatment of patients with acute respiratory distress syndrome: A clinical review. *BioMed Research International*, *2015*, 653750. [CrossRef]

Haköksüz, M., Kılıç, S., & Saraç, F. (2020). Coronaviruses and SARS-CoV-2. *Turkish Journal of Medical Sciences*, *50*(SI–1), 549–556. [CrossRef]

Hathaway, D., Pandav, K., Patel, M., Riva-Moscoso, A., Singh, B. M., Patel, A., Min, Z. C., Singh-Makkar, S., Sana, M. K., Sanchez-Dopazo, R., Desir, R., Fahem, M. M. M., Manella, S., Rodriguez, I., Alvarez, A., & Abreu, R. (2020). Omega 3 fatty acids and covid-19: A comprehensive review. *Infection and Chemotherapy*, *52*(4), 478–495. [CrossRef]

Hoffmann, M., Kleine-Weber, H., Schroeder, S., Krüger, N., Herrler, T., Erichsen, S., Schiergens, T. S., Herrler, G., Wu, N. H., Nitsche, A., Müller, M. A., Drosten, C., & Pöhlmann, S. (2020). SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell*, *181*(2), 271–280.e8. [CrossRef]

Institute of Medicine. (2005). *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids*. The National Academies Press. [CrossRef]

Jing, K., Wu, T., & Lim, K. (2013). Omega-3 polyunsaturated fatty acids and cancer. *Anti-Cancer Agents in Medicinal Chemistry*, *13*(8), 1162–1177. [CrossRef]

Kagawa, Y. (2022). Influence of nutritional intakes in Japan and the United States on COVID-19 infection. *Nutrients*, *14*(3), 633. [CrossRef]

Köhler, A., Heinrich, J., & von Schacky, C. V. (2017). Bioavailability of dietary omega-3 fatty acids added to a variety of sausages in healthy individuals. *Nutrients*, *9*(6), 629. [CrossRef]

Kranz, S., Huss, L. R., & Dobbs-Oates, J. (2015). Food sources of EPA and DHA in the diets of American children, NHANES 2003–2010. *BAOJ Nutrition*, *1*(1), 1–12. [CrossRef]

Kris-Etherton, P. M., Harris, W. S., Appel, L. J., & AHA Nutrition Committee. American Heart Association. (2003). Omega-3 fatty acids and cardiovascular disease: New recommendations from the American Heart Association. *Arteriosclerosis, Thrombosis, and Vascular Biology*, *23*(2), 151–152. [CrossRef]

Louca, P., Murray, B., Klaser, K., Graham, M. S., Mazidi, M., Leeming, E. R., Thompson, E., Bowyer, R., Drew, D. A., Nguyen, L. H., Merino, J., Gomez, M., Mompeo, O., Costeira, R., Sudre, C. H., Gibson, R., Steves, C. J., Wolf, J., Franks, P. W., Ourselin, S., et al. (2021). Modest effects of dietary supplements during the COVID-19 pandemic: Insights from 445 850 users of the COVID-19 Symptom Study app. *BMJ Nutrition, Prevention and Health*, *4*(1), 149–157. [CrossRef]

Maki, K. C., & Dicklin, M. R. (2019). Strategies to improve bioavailability of omega-3 fatty acids from ethyl ester concentrates. *Current Opinion in Clinical Nutrition and Metabolic Care*, *22*(2), 116–123. [CrossRef]

Nabavi, S. F., Bilotto, S., Russo, G. L., Orhan, I. E., Habtemariam, S., Daglia, M., Devi, K. P., Loizzo, M. R., Tundis, R., & Nabavi, S. M. (2015). Omega-3 polyunsaturated fatty acids and cancer: Lessons learned from clinical trials. *Cancer and Metastasis Reviews*, *34*(3), 359–380. [CrossRef]

Ramírez-Santana, M., Zapata Barra, R., Ñunque González, M., Müller, J. M., Vásquez, J. E., Ravera, F., Lago, G., Cañón, E., Castañeda, D., & Pradenas, M. (2022). Inverse association between Omega-3 index and severity of COVID-19: A case–control study. *International Journal of Environmental Research and Public Health*, *19*(11), 6445. [CrossRef]

Schönfeldt, H., Pretorius, B., & Hall, N. (2016). Bioavailability of nutrients. In Benjamin Caballero, Paul M. Finglas and Fidel Toldrá (eds.) *Encyclopedia of Food and Health*. Elsevier, 401-406. [CrossRef]

Sears, B. (2018). Appropriate doses of omega-3 fatty acids for therapeutic results. *College Review*, *6*(4), e2578.

Shereen, M. A., Khan, S., Kazmi, A., Bashir, N., & Siddique, R. (2020). COVID-19 infection: Emergence, transmission, and characteristics of human coronaviruses. *Journal of Advanced Research*, *24*, 91–98. [CrossRef]

Surette, M. E. (2008). The science behind dietary omega-3 fatty acids. *Canadian Medical Association Journal*, *178*(2), 177–180. [CrossRef]

Swanson, D., Block, R., & Mousa, S. A. (2012). Omega-3 fatty acids EPA and DHA: Health benefits throughout life. *Advances in Nutrition*, *3*(1), 1–7. [CrossRef]

Szabó, Z., Marosvölgyi, T., Szabó, É., Bai, P., Figler, M., & Verzár, Z. (2020). The potential beneficial effect of EPA and DHA supplementation managing cytokine storm in coronavirus disease. *Frontiers in Physiology*, *11*, 752. [CrossRef]

Tang, D., Comish, P., & Kang, R. (2020). The hallmarks of COVID-19 disease. *PLOS Pathogens*, *16*(5), e1008536. [CrossRef]

Weill, P., Plissonneau, C., Legrand, P., Rioux, V., & Thibault, R. (2020). May omega-3 fatty acid dietary supplementation help reduce severe complications in covid-19 patients? *Biochimie*, *179*, 275–280. [CrossRef]

WHO. (2020). Listings of WHO's Response to COVID-19. Retrieved from https://www.who.int/news/item/29-06-2020-covidtimeline (Access date: March 21, 2021).

WHO. (2022). WHO Coronavirus (COVID-19) Dashboard. Retrieved from https://covid19.who.int/ (Access date: June 16, 2022).

Zabetakis, I., Lordan, R., Norton, C., & Tsoupras, A. (2020). Covid-19: The inflammation link and the role of nutrition in potential mitigation. *Nutrients*, *12*(5), 1466. [CrossRef]