



## Effects of $\omega$ -3 fatty acids and ratio of $\omega$ -3/ $\omega$ -6 for health promotion and disease prevention

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### Abstract

Awareness of the role of essential fatty acids in human health and disease prevention has been increasing among the population over the past decades. It is known that the positive correlation of essential fatty acid content with a decrease in cardiovascular morbidity and mortality, infant development, brain and vision functioning, arthritis, hypertension, diabetes mellitus, and neurological/neuropsychiatric disorders. Rich sources of essential fatty acids are fish, fish oil, and some vegetable oils. In this paper, the average content of linoleic and  $\alpha$ -linolenic acids in oils (g/100 g of fat) and their ratio is presented. In Kazakhstan, among vegetable oils, sunflower oil is the most commonly consumed, in which the ratio  $\omega$ -6 to  $\omega$ -3 on average is about 220:1, which exceeds all recommended norms. Based on the examination of literary data on this topic, the desk-based research approach was used in this paper. According to the results, statistical data on the number of diseases of the cardiovascular system and diabetes mellitus are confirmed by studies on the positive relationship between PUWC and the development of these diseases, which indicates the need to conduct more studies on the ratio of  $\omega$ -6 to  $\omega$ -3 in the diets. The objective of this research is to encourage scientists to increase their basic grasp of biochemistry in order to improve health and prevent fatty acid illness.

**Keywords:**  $\omega$ -3,  $\omega$ -6 fatty acids, ratio of fatty acids, effect on organism.

**Practical Application:** The recommended ratios of  $\omega$ -3 and  $\omega$ -6 fatty acids are different in different background diets with different amounts of  $\omega$ -6 and  $\omega$ -3 fatty acids. The optimal range reflecting the absolute requirements or optimal ratios of fatty acids is not defined, as are the requirements for types of food fats. These disagreements motivate researchers to improve fundamental understanding of biochemistry to promote health and prevent fatty acid disease.

### 1 Introduction

A fatty acid is a carboxylic acid with a long aliphatic chain that is either saturated or unsaturated in chemistry, particularly biochemistry (Chinenye et al., 2019). The majority of naturally occurring fatty acids contain a chain with an even number of carbon atoms, ranging from 4 to 28. Fatty acids are a key component of lipids in some species, such as microalgae, but they are not found in their freestanding form (Kimura et al., 2020). Instead, they are present as three types of esters (Gao et al., 2018; Zhang et al., 2018): triglycerides, phospholipids, and cholesteryl esters. Fatty acids are significant nutritional sources of fuel for animals as well as structural components of cells in any of these forms (Pierce & McWilliams, 2014). Since the 1970s, researchers have found that Eskimos living in Greenland rarely suffer from cardiovascular disease, and people have begun to gradually study omega-3 fatty acids (Fodor et al., 2014; Nobmann, 1996; Simopoulos, 2002). Researchers from different countries have shown that omega-3 fatty acids have anti-inflammatory, anti-thrombus, anti-heart rhythms, reduce blood lipid levels, and have vasodilating properties (Adili et al., 2018; Calder, 2012; Holub & Holub, 2004; Massaro et al., 2008).

The Food and Agriculture Organization of the United Nations issued a recommendation on food fats and oils in October 1993, according to which, as essential omega-3 and omega-6 fatty acids, fatty acids play an important role in the structure of cell membranes, as well as eicosanoids (arachidic acids) (World Health Organization, 1994).

The Food and Agriculture Organization's recommendation for essential fatty acid consumption is that the ratio of omega-6 to omega-3 in the diet should be 5:1 or 10:1. If this ratio is violated, these individuals should consume richer omega-3, such as green leafy vegetables, legumes, fish, and other seafood (Sheppard & Cheatham, 2018; Simopoulos et al., 1999). Particular attention is paid to ensuring adequate consumption of essential fatty acids during pregnancy and breastfeeding to meet the development needs of the fetus and child (Sverguzova et al., 2021). Omega-3 fatty acids are long-chain polyunsaturated fatty acids (PUFA) that are found in plants and marine organisms. The three main omega-3 fatty acids are docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), and alpha-linolenic acid (ALA) (Judge, 2018; Kang, 2004). Alpha-linolenic acid (ALA) is

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plant-based essential omega-3 polyunsaturated fatty acids with three double bonds (Blondeau et al., 2015).

$\alpha$ -linolenic acid makes 67% in perilla oil, 55% in linseed oil, 42% in peony oil, 32% in sea buckthorn oil, 20% in Bama hemp oil, 10% in rapeseed oil, 8% in soybean oil, and 50% in grape oil (Su et al., 2018). Currently, the edible oil with the most  $\alpha$ -linolenic acid found is perilla seed oil. The second and third are derived from animals and fish, eicosapentaenoic acid seals (eicosapentaenoic acid, EPA, containing five unsaturated bonds) and docosahexaenoic acid (docosahexaenoic acid, DHA, containing six unsaturated bonds) (Abdelhamid et al., 2018; Covington, 2004; Gutiérrez et al., 2019; Shahidi & Ambigaipalan, 2018).

Since PUFA gives rise to a variety of biologically active compounds, which all play an important role in pathological and physiological processes, it is necessary to have a proper understanding of the contribution that these active compounds have to the concurrent increase in inflammatory diseases observed with the imbalance in the body (Patterson et al., 2012; Zárate et al., 2017).

The increase in  $\omega$ -6: $\omega$ -3 PUFA ratio, characteristic of the Western diet, can enhance inflammatory processes and therefore predispose or exacerbate many inflammatory diseases (Johnson et al., 2019). A change in the aforementioned ratio and an increase in the intake of  $\omega$ -6 PUFA change the production of important mediators and regulators of inflammation and immune responses in the direction of the pro-inflammatory profile. It should be noted that the unbalanced dietary intake of  $\omega$ -6: $\omega$ -3 PUWC is harmful to human health, and therefore the effect of dietary supplements with  $\omega$ -3 PUWC on the relief of inflammatory diseases should be more thoroughly investigated (Patterson et al., 2012).

The goal of this study is to encourage scientists to increase their basic grasp of biochemistry in order to improve health and prevent fatty acid illness.

## 2 Literature review

Studies have shown that saturated fatty acids have beneficial health effects, and as PUFAs,  $\omega$ -3 fatty acids have many health benefits. Various data suggest that a decrease in Omega-3 fatty acid concentration may cause mood disorders (Diniz et al., 2004; Kris-Etherton et al., 2004; Lunn & Theobald, 2006; Montiel-Rojas et al., 2020; Weaver et al., 2008). Some preliminary research findings suggest that they can effectively treat various mental disorders such as bipolar disorder, schizophrenia, and dementia. For pregnant and nursing women, this is a safe and effective treatment (Ströhle, 2019).

Many studies have shown that eating foods with long-chain omega-3 fatty acids, eicosapentaenoic acid (EPA), and DHA (e.g., fatty fish) is associated with a reduced risk of coronary heart disease (Alexander et al., 2017; Covington, 2004; Harris et al., 2008; Holub & Holub, 2004; Wall et al., 2010). Studies have shown that essential fatty acids are extremely important for the growth and development of fetuses and infants, especially for the development of the brain and vision. Women who eat well during pregnancy deposit approximately 2.2 grams of

essential fatty acids daily in mother and baby tissues (Chavan-Gautam et al., 2018; Duttaroy & Basak, 2020; Tressou et al., 2019; Wadhwani et al., 2018).

In 2004, the US National Food and Drug Administration (FDA) published an announcement that "omega-3 fatty acids are a quality healthy food that can reduce the risk of coronary heart disease" (Agarwal et al., 2019; Baum, 2020; Bone & France, 2009; Matthias, 2021).

Compared to the scientific and research growth of  $\omega$ -3 in the world, Kazakhstan citizens are still at an impasse about the health benefits of  $\omega$ -3, and the concept is still unfamiliar, and few Kazakh scientists study it (Gordeyeva et al., 2017; Martin & Li, 2017; Mikhajlova & Sokolova, 2001). Although  $\omega$ -3 fatty acids are important nutrients for humans, they cannot be synthesized in the human body and must be derived from food. Dr. Jing X. Kang, who is director of the Harvard Center for Fatty Acid Research, noted that fatty acids, as well as vitamins and amino acids, are one of the most important nutrients in the human body. PUFAs  $\omega$ -3 are one of two essential fatty acids that the human body cannot synthesize and that must enter the body with food, and the other -  $\omega$ -6 fatty acids (Meester & Watson, 2008; Delpech et al., 2015; Liu et al., 2014; Luo et al., 2021; Wu et al., 2016; Yin et al., 2016).

Employing genetic technology to implant the Fat-1 nematode gene (a type of worm, *C. elegans* in English) in mice has been studied (Lee et al., 2016). This gene can convert omega-6 fatty acids in mice into omega-3 fatty acids. Using this technology, steak and eggs will become good food for the heart, which is undoubtedly a revolutionary change for animal husbandry, and the food industry (Li et al., 2018).

A research has shown that there is a link between an imbalance of  $\omega$ -3 in the diet and impaired brain function and cognitive diseases (Chang et al., 2009). The brain contains more than 100 billion cells, and  $\omega$ -3 fatty acids are the main materials that make up these cells. These fats bind to the cell membrane and increase cell membrane fluidity, which is very important for maintaining normal brain cells (Calder, 2010). Higher membrane fluidity helps the brain transform and adapt to new information. In addition, the integration of omega-3 into the cell membrane also helps to maintain the function of neurotransmitter receptors and promotes the transmission of information in the brain (Tanaka et al., 2012). A neurotransmitter is a chemical in the brain that is used to transmit information between the brain and the human body. Preliminary studies have shown that  $\alpha$ -3 can stimulate brain growth factor secretion (Wu et al., 2004). This, in turn, will contribute to the synthesis of brain messengers and reduce the destruction of brain messengers.

The importance of  $\omega$ -3 fatty acids for human health has been established by epidemiological studies showing an association between an enriched  $\omega$ -3 diet and the prevention of certain diseases, such as cardiovascular diseases and myocardial infarction (Das, 2000; Kromann & Green, 1980; Von Schacky & Harris, 2007), psoriasis (Zulfakar et al., 2007), bowel diseases (Diamond et al., 2008), treatment and prevention of mental diseases (Song & Zhao, 2007), prevention of several types of

cancer (Calviello et al., 2007; Chen et al., 2007) or bronchial asthma (Das et al., 2012).

Omega-3 is an essential fatty acid and must be obtained from food. They are also important for healthy brain function but not as important as ω-3. Omega-3 is a precursor to anti-inflammatory hormones and helps relieve inflammation in the brain (Wyss-Coray & Rogers, 2012).

ω-6 and ω-3 PUFAs are essential fatty acids to be obtained from the diet and cannot be obtained by humans and other mammals due to the absence of endogenous enzymes for desaturation ω-3 (Kang, 2003; Simopoulos, 2001). Thanks to agribusiness and modern agriculture, Western diets contain an excessive amount of ω-6 PUFA, but a very low level of ω-3 PUFA, which leads to an unhealthy ratio of ω-6:ω-3 (20:1) instead of 1:1, which was in the process of evolution in humans (Simopoulos, 2001, 2008).

If both ω-3 and ω-6 are present, they will compete for conversion to their respective final products, so the ω-6:ω-3 ratio directly affects the type of eicosanoids produced. This competition was considered important when thromboxane was found to be a platelet accumulation factor, leading to thrombosis (Balić et al., 2020). It was also found that leukotrienes - organic compounds, a group of lipid highly active substances formed in the body from arachidonic acid containing a 20-membered carbon chain - are important for the immune/inflammatory system and, therefore are related to arthritis, lupus and asthma (Haeggström, 2018; Michael et al., 2019; Sasaki & Yokomizo, 2019; Yokomizo et al., 2018). These discoveries led to a greater interest in finding ways to control the synthesis of ω-6 eicosanoids. The easiest way is to consume more ω-3 and less ω-6 fatty acids. EPA forms powerful anti-inflammatory nano molecules called resolvins in the body (Das, 2021; Lee & Surh, 2012). Later, it was found that ω-3 also converts to other anti-inflammatory molecules called omega-3-oxylipins (Shearer et al., 2010). In general, the positive health effects of ω-3 fatty acids are associated with the inhibition or modulation of eicosanoid pathways that result in a change in inflammatory responses and the associated protein expression activity and modulation of molecules or enzymes associated with different signaling pathways involving normal and pathological cell function, the inclusion of ω-3 fatty acids in membrane phospholipids, and direct effects on gene expression (BourBour et al., 2020; Calder et al., 2020; Das, 2020; Gombart et al., 2020). Since all these pathways are very interactive, the biological potential of ω-3 fatty acids for health and disease should be due to a variety of coordinated mechanisms (Seo et al., 2005). Therefore, ω-3 fatty acids are practically functional foodstuffs.

Thus, the unbalanced ratio ω-6:ω-3 in favor of ω-6 PUFA is highly prothrombotic and proinflammatory, which contributes to the spread of atherosclerosis, obesity, and diabetes (Kang, 2003; Shahidi & Ambigaipalan, 2018; Simopoulos, 2001, 2008, 2013). In fact, regular intake of diets rich in ω-3 PUFA was associated with a low incidence of these diseases, especially among Icelandic, Inuit, and Native American populations in Alaska (Adler et al., 1994; Kromann & Green, 1980; Schraer et al., 1999). However, the use of fish oil as the main source of omega-3 PUFA for the treatment of type 2 diabetes has not always been

successful (Kromhout & Goede, 2014; Mozaffarian & Rimm, 2006; Nettleton & Katz, 2005).

Blood levels ω-3 may vary depending on lifestyle (e.g., fish intake), geographical and genetic causes (Superko et al., 2014). According to the studies on erythrocyte index, the average omega-3 index content among the Kazakh population was  $2.08 \pm 0.92\%$  (Raushan & Lazzat, 2019) lower than in other countries: in Russia from 1.12% to 6.4%, averaging 3.74% (Aarsetoy et al., 2011), in Germany  $3.7 \pm 1.0\%$  (Berliner et al., 2019).

Early epidemiological studies showed that a high level of ω-6 fats could worsen cardiovascular risk by increasing inflammation, and ingestion of ω-3 PUFA, on the contrary, has an anti-inflammatory effect, has antioxidant and metabolic effects, and high intake of ω-3 PUFA reduces the risk of cardiovascular disease (Barrea et al., 2020; Innes & Calder, 2020; Rogero et al., 2020; Thirumdas et al., 2021).

According to author, Narinder Kaur of Punjab Agricultural University, ω-3 fatty acids can have beneficial effects on heart health and possibly other diseases such as cancer, diabetes, and neurological disorders (Kaur et al., 2014). The anti-inflammatory effect of [omega]-3 fatty acids can also be used in the treatment of inflammatory diseases. Individuals at special stages of the life cycle, such as pregnant/nursing women, infants, and children, may also benefit from the intake of [omega] - 3 fatty acids in adequate amounts. The authors also provided the content of [omega] - 6 and [omega] - 3 in vegetable oils, which is shown in Table 1.

A higher ratio of omega-6 to omega-3 will lead to the body becoming pro-inflammatory. Studies have shown that a high ratio of ω-6 to ω-3 is associated with worsening inflammation (including brain inflammation) (Balić et al., 2020; Hsieh et al., 2020; Limdi, 2018). Since omega-3 and omega-6 in the cell membrane will compete, it is very important to properly balance these two substances' ratio to stimulate the anti-inflammatory state (Patterson et al., 2012).

Although fatty acids ω-3, ω-6 have different effects on the human body, there is strong evidence that in order to maintain the overall health of the heart and the overall physical and mental health of people in accordance with the balance, proportional consumption of essential and essential fatty acids is very necessary (Weill et al., 2020). According to the American Dietary Association study, adults should consume 20-35% of their energy from food fats while avoiding ("harmful") saturated fats and trans fats. Focus on fatty acid intake ω-3 (Otto et al., 2013).

The content of omega-6 fatty acids in a typical American diet is often 14-25 times greater than the content of ω-3 fatty acids, while the distribution of ω-6 and ω-3 fatty acids in the Mediterranean diet is in healthier equilibrium. Studies have shown that people following a Mediterranean diet are less susceptible to heart disease. The meat content in the Mediterranean diet is low (the meat contains more fatty acids ω-6, while the beef fed by grass has the best ratio of fatty acids ω-3 and ω-6), and emphasizes that the consumption of more omega-3 fatty acids (Lorgeril, 2013; Trichopoulou et al., 2005).

Maintenance of the general state of health should ensure the balance of  $\omega$ -6 and  $\omega$ -3 fatty acids. The ratios  $\omega$ -6 and  $\omega$ -3 should be between 2:1 and 4:1, and some health teachers advocate even lower ratios. Studies have shown that a 2-3:1 ratio between  $\omega$ -6 and  $\omega$ -3 helps reduce inflammation in patients with rheumatoid arthritis, a ratio of 5:1 has a beneficial effect on asthma patients, and the ratio is 10:1 Has a negative effect: the ratio 2.5:1 has a reduced effect on the proliferation of rectal cells in patients with colorectal cancer, but the ratio 4:1 has no effect (Papandreou et al., 2020; Zong et al., 2021).

### 3 Research methods

In this article, the desk-based research method was applied based on the analysis of literary data on this issue. Secondary research, often known as desk research, is a type of research that makes use of previously collected data. To improve the overall efficacy of research, existing data is summarized and compiled. Research information released in research reports and other comparable papers is considered secondary research.

Public libraries, websites, and data from previously completed surveys, among other sources, can make these papers available. Some government and non-government entities also keep data that may be retrieved and utilized for research reasons. Secondary research is significantly more cost-effective than primary research because it uses data that already exists instead of primary research, which requires organizations or enterprises to collect data themselves or hire a third party to do it on their behalf. Secondary research is inexpensive, which is one of the reasons why it is a popular option for many firms and organizations. Not every company can afford to spend a large quantity of money on research and data collection. Because data may be accessed while sitting at a desk, secondary research is sometimes known as “desk research.”

### 4 Results and discussion

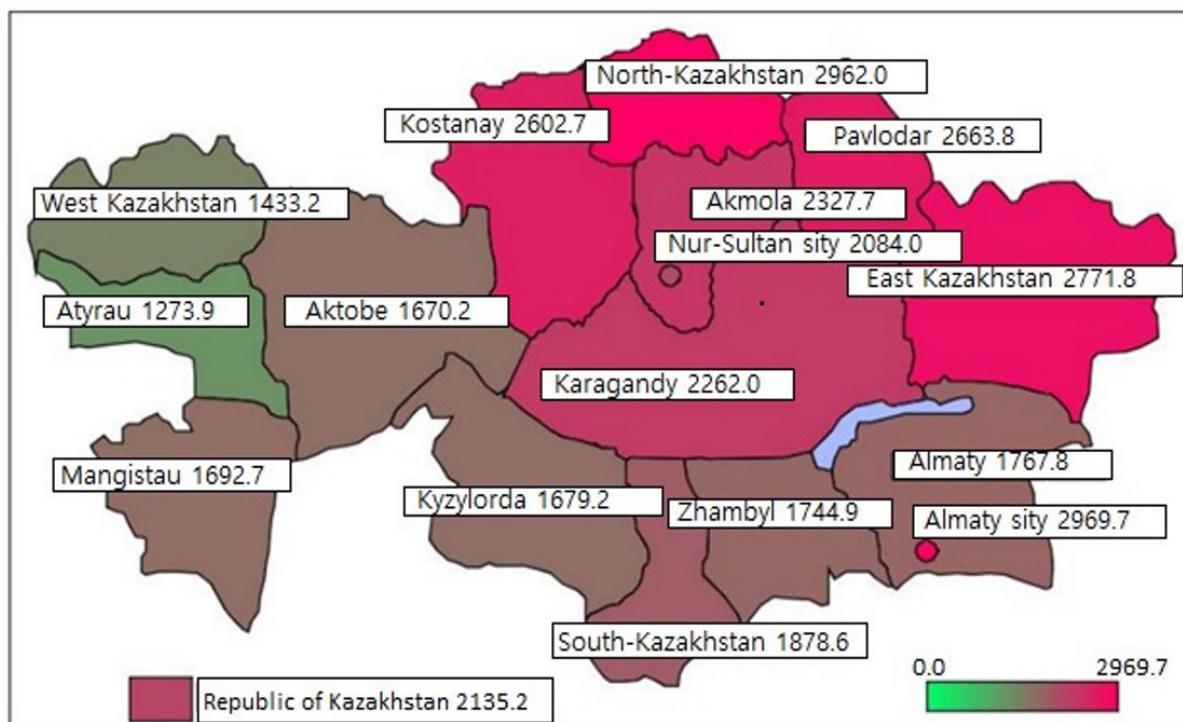
Over the past few decades, there have been extreme qualitative changes in nutrition with an increased level of fatty acid intake (Simopoulos, 2011). Today, industrialized societies are characterized by an increase in the consumption of saturated fats,  $\omega$ -6 PUFA, and trans-fatty acids, as well as an overall decrease in the consumption of omega-3 PUFA (Molendi-Coste et al., 2010). Fatty acids currently account for 28-42% of the total energy consumed by the European population (Linseisen et al., 2009; Molendi-Coste et al., 2010), while in ancestral nutrition, fatty acid intake was only about 20-30% of the total energy (Anderson & Ma, 2009; Eaton et al., 2010; Molendi-Coste et al., 2010). As a result of the increased consumption of LA-rich vegetable oils associated with the Western diet, the consumption of  $\omega$ -6 PUFA became much higher than the consumption of  $\omega$ -3 PUFA (Anderson & Ma, 2009). The optimal intake in the diet of the ratio  $\omega$ -6:  $\omega$ -3 should be about 1-4:1. However, according to the nutritional changes described above in the Western diet, this ratio has now increased to 10:1 up to 20:1 (Molendi-Coste et al., 2010).

The ratio  $\omega$ -6 and  $\omega$ -3 in the modern diet reach 15:1. Studies have shown that this is most beneficial for health when the ratio of two is close to 1:1 (Simopoulos, 2003). This can be achieved by eating more foods containing  $\omega$ -3 (e.g., cold-water fish), taking the necessary additives, and reducing the consumption of processed foods and vegetable oils.

According to the data, sunflower oil is the leader in producing and consuming vegetable oils in Kazakhstan (Abduhakim, 2019; Mukhametov et al., 2020). And the ratio  $\omega$ -6 to  $\omega$ -3 in sunflower oil averages about 220:1 (Table 1). This figure exceeds all recommended standards. According to the obtained data of the study, a positive association between PUFA and the development of cardiovascular disease and diabetes mellitus is confirmed by statistics on these diseases in the Republic of Kazakhstan.

**Table 1.** The average content of linoleic (LA 18:2 n-6) and  $\alpha$ -linolenic (ALA 18:3 n-3) acids in oils (g/100 g fat) and their ratio.

Sr, No,	Oil	LA 18:2(n-6)	ALA 18:3(n-3)	Total unsaturated fatty acids	Ratio LA 18:2(n-6) / ALA 18:3(n-3)
1	Soybean (Liou et al., 2007)	50.8	6.8	80.7	7.5:1
2	Cottonseed (Matthäus & Özcan, 2015)	50.3	0.4	69.6	125.7:1
3	Corn (Vos & Cunnane, 2003)	57.3	0.8	82.8	71.6:1
4	Safflower (Srinivas et al., 1999)	73	0.5	86.3	146:01:00
5	Sunflower (Delplanque, 2000)	66.4	0.3	88.5	221.3:1
6	Sesame (Chellamuthu et al., 2017)	40	0.5	80.5	80:01:00
7	Olive (Svensson et al., 2011)	8.2	0.7	81.4	11.7:1
8	Peanut (Konuskan et al., 2019)	31	1.2	77.8	25.8:1
9	Rapeseed (Zeroerucicacid) (Nguemeni et al., 2010)	22.2	11	88	02:01
10	Linseed (Dadd, 2019; Guu et al., 2019)	16	57	73.0	1:3.5



**Figure 1.** The Map of the RK areas on prevalence sugar diabetes in 100 000 population (Nurgaliyeva et al., 2020).

According to data in Kazakhstan, in absolute figures, more than 40 thousand cases of strokes are recorded annually in our country, of which only 5 thousand died in the first ten days and another 5 thousand during the first month after a stroke (Doskeyeva et al., 2018; Tokshilykova et al., 2020).

The incidence of diabetes mellitus in Kazakhstan, according to the national register of the Republic of Kazakhstan, takes 3rd place in the Republic after cardiovascular and oncological diseases (Mukasheva et al., 2019). The map (Figure 1), which is made according to the National Register of the Republic of Kazakhstan, shows the number of officially registered patients suffering from diabetes.

The most common areas for diabetes mellitus include the northern regions of the country and Central Kazakhstan, including the western regions. As data of research papers on actual nutrition in a sample of the Kazakh population show imbalance in the consumption of food substances, sources of omega-3. There is also high consumption of harmful carbohydrates and saturated fats in a large number of confectionery products and low consumption of useful fish, nuts, raw fruits, and vegetables (Raushan & Lazzat, 2019). Thus, ongoing innovation and a growing body of scientific evidence to support nutritional guidelines for  $\omega$ -3 and  $\omega$ -6 fatty acids can help populations achieve optimal health.

## 5 Conclusion

Increasing number of clinical and experimental studies on  $\omega$ -6, and  $\omega$ -3 FA reflects the growing awareness and importance of these components in our diet.  $\omega$ -3 FA, in a certain ratio with  $\omega$ -6

FA, is important not only for normal growth and development but also for the prevention and treatment of certain diseases.

However, the recommended ratios of  $\omega$ -3 and  $\omega$ -6 fatty acids are different in different background diets with different amounts of  $\omega$ -6 and  $\omega$ -3 fatty acids. The optimal range reflecting the absolute requirements or optimal ratios of fatty acids is not defined, as are the requirements for types of food fats. These disagreements motivate researchers to improve fundamental understanding of biochemistry to promote health and prevent fatty acid disease.

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