زانکۆی سەلاحەدین ـ هەولێر
Salahaddin University- Erbil

A Topical Update on the Effects omega-3 Fatty Acids on Alzheimer's Disease

Research Project Submitted to the department of Chemistry in partial fulfillment of the requirements for the degree of BSc. In (Chemistry)

By:

Lezan Mohammad Ebrahem

Supervised By:

Asst.prof. Lutfia Mohammad Hassan

April-2024

CERTIFICATE

This project has been written under my supervision and has been submitted for the award of the degree of BSc. in **chemistry** with my approval as supervisor

Signature Name: **Asst.prof. Lutfia Mohammad Hassan**

Date: / / 2024

I confirm that all requirements have been completed.

Research Project Lecturer

Signature:

Name: **Asst. Prof. Dr. Dler D. Kurda**

Date / / 2024

Dedication

The Salahaddin University, my second magnificent home.

My great parents, who never stop giving of themselves in countless ways.

My beloved brothers and sisters.

To all my family and my friends who encourage and support me.

All the people in my live who support me in academic life.

Acknowledgements

First and foremost, I must acknowledge my limitless thanks to Allah, the Ever Magnificent; the Ever-Thankful, for His help and blessing. I owe a deep debt of gratitude to the chemistry department and Salahaddin University for giving us an opportunity to complete this work. I am very appreciative of my colleagues in the chemistry department. I am grateful to some people, who worked hard with me from the beginning till the completion of the present research particularly my supervisor (Asst.prof. Lutfia Mohammad Hassa), has been always generous during all phases of the research. I would like to take this opportunity to say warm thanks to all my beloved friends, who have been so supportive along the way of doing my thesis. I also would like to express my wholehearted thanks to my family for the generous support they provided me throughout my entire life and particularly through the process of pursuing the thesis. Last but not least, deepest thanks go to all people who took part in making this thesis real.

Lezan Mohammad Ebrahem

Table of Contents	
Subject	**Page No**

LIST OF FIGURE

LIST OF TABLES

List of Abbreviations

NO	Abbreviations	Stands for
1	AD	Alzheimer's disease
2	ADHD	Attention-deficit/hyperactivity disorder
3	ALA	alpha-linolenic acid
5	DHA	Docosahexanoic acid
6	EPA	eicosapentaenoic acid
7	FA	Fatty acid
8	FAs	Fatty acid synthase
9	HUFAs	Highly unsaturated fatty acids
10	LA	Linoleic acid
11	LCFAs	Long-chain fatty acids
12	LDL	Low-density lipoprotein
13	MUFAs	Monounsaturated fatty acids
14	n-3	Position of first double bond
15	PUFAs	Polyunsaturated fatty acids
16	SFAs	Saturated fatty acids
17	UFAs	Unsaturated fatty acids
18	ω-3	Omega-3
19	ω-6	Omega-6

Abstract

Omega-3 fatty acids are essential for brain growth and development. They play an important role throughout life, as critical modulators of neuronal function and regulation of oxidative stress mechanisms, in brain health and disease. Docosahexanoic acid (DHA), the major omega-3 fatty acid found in neurons, has taken on a central role as a target for therapeutic intervention in Alzheimer's disease (AD). A plethora of in vitro, animal model, and human data, gathered over the past decade, highlight the important role DHA may play in the development of a variety of neurological and psychiatric disorders, including AD. Cross sectional and prospective cohort data have demonstrated that reduced dietary intake or low brain levels of DHA are associated with accelerated cognitive decline or the development of incipient dementia, including AD. Several clinical trials investigating the effects of omega-3 fatty acid supplementation in AD have been completed and all failed to demonstrate its efficacy in the treatment of AD. However, these trials produced intriguing data suggesting that the beneficial effects of omega-3 fatty acid supplementation may depend on the stage of disease, other dietary mediators.

Key Words: Alzheimer's disease, Omega-3, Fatty acid

Introduction

Omega-3 fatty acids, primarily found in fish and nuts, have become a focal point in the realm of Alzheimer's disease (AD) research. The two significant constituents, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), play pivotal roles in brain health by influencing cell membrane structure and function(Dyall, 2015). The allure of omega-3 fatty acids lies in their potential neuroprotective effects, attributed to their well-documented anti-inflammatory and antioxidant properties(Morris et al., 2016). These qualities raise the prospect of these fatty acids providing a defense against neurodegenerative conditions, including Alzheimer's. The intricate relationship between oxidative stress, inflammation, and AD progression underscores the significance of exploring substances like omega-3s that can potentially modulate these processes.

Observational studies have tentatively suggested a correlation between increased omega-3 intake and a lower risk of cognitive decline, providing a promising avenue for investigation(Schaefer et al., 2006). However, the translation of these findings into a concrete cause-and-effect relationship necessitates rigorous clinical trials. The scientific community is actively engaged in unraveling the nuanced mechanisms through which omega-3s exert their influence on brain health and their potential impact on the complex pathology of Alzheimer's. It is paramount to approach the discussion with a balanced perspective. While incorporating omega-3-rich foods into the diet is generally advocated for overall health, caution is warranted in placing undue expectations on dietary supplements alone to prevent or treat Alzheimer's. The multifaceted nature of maintaining cognitive function emphasizes the importance of holistic lifestyle factors, including regular physical activity and sustained cognitive engagement (Schaefer et al., 2006).

Chapter one

1.1 Fatty acid

The fatty acid molecule consists of a long hydrocarbon chain with a polar carboxyl group at its end (Puri, 2011). The carboxylate ion has polar characteristics, with high affinity for water (hydrophilic). Being non-polar in nature, hydrocarbon chain accounts for predominantly non-polar character of the fatty acid molecule. Thus, a fatty acid molecule contains both polar (hydrophilic) and non-polar (hydrophobic) regions; such molecules are called amphipathic molecules. Naturally occurring fatty acids contain even number of carbon atoms (most contain 14 to 24). Of these, most abundant are the fatty acids containing 16 or 18 carbon atoms. The fatty acids with hydrocarbon chains containing one or more double bonds are called unsaturated fatty acids, whereas those lacking any double bonds are referred to as saturated fatty acids(Puri, 2011).

Fatty acids, both free and as part of complex lipids, play a number of key roles in metabolism – major metabolic fuel (storage and transport of energy) (Rustan and Drevon, 2001). the most important dietary sources of fatty acids are vegetable oils, dairy products, meat products, grain and fatty fish or fish oils, Eicosapentaenoic acid (EPA; 20:5 ω-3) and docosahexaenoic acid (DHA; 22:6 ω-3) are major fatty acids of marine algae, fatty fish and fish oils; for example, DHA is found in high concentrations, especially in phospholipids in the brain, retina and testes (Rustan and Drevon, 2001).

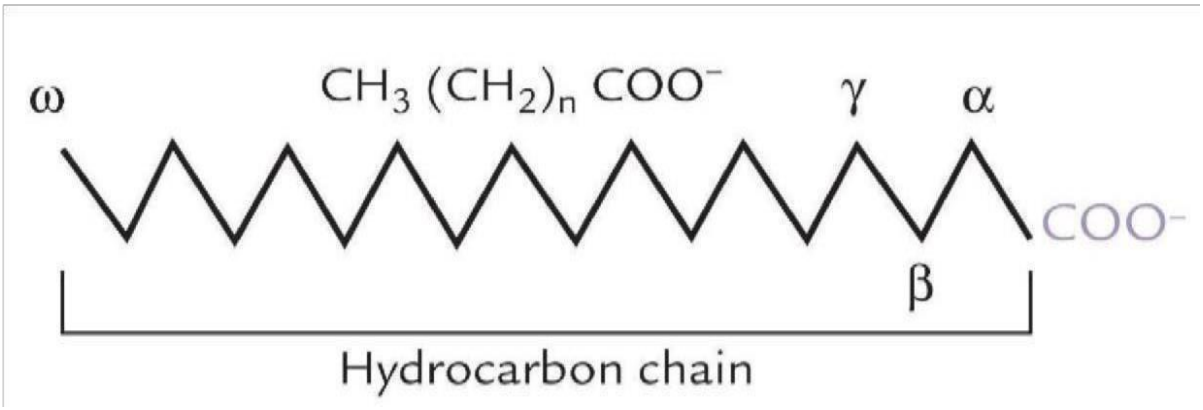

Fig 1. Structure of a fatty acid (Puri, 2011).

1.2 Fatty acid nomenclature

The abbreviated designation includes the number of carbon atoms, number of double bonds, and locations of the double bonds in parenthesis. For example, αlinolenic acids, is recorded as 18:3(9,12,15), or as 18:3 (n-3) (Doc. RNDr. Jiří Dostál, 2014).

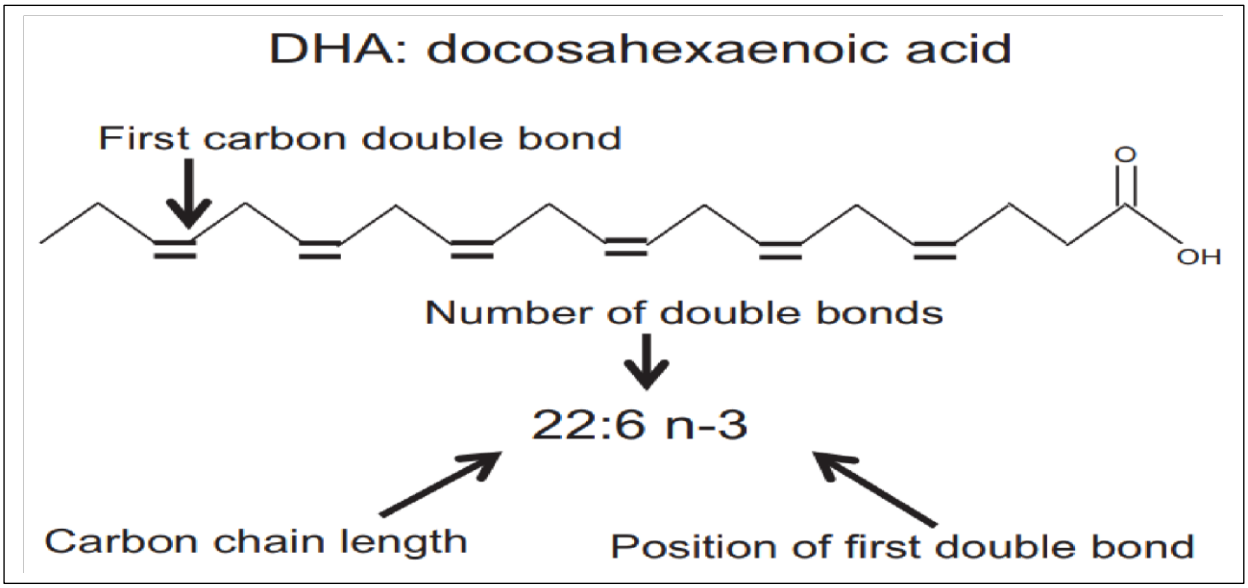

Fig 2. Nomenclature docosahexaenoic acid

1.3 Type fatty acid

1.3.1 Carbon chain length (Twining et al., 2016)

- Long-chain fatty acids (LCFAs): fatty acids with more than twenty carbon atoms

1.3.2 Number of double bonds (Twining et al., 2016)

- Saturated fatty acids (SFAs): fatty acids without double bonds between carbon atoms
- Unsaturated fatty acids (UFAs): fatty acids with at least one double bond between carbon atoms
- Monounsaturated fatty acids (MUFAs): fatty acids with one double bond between carbon atoms
- Polyunsaturated fatty acids (PUFAs): fatty acids with multiple double bonds between carbon atoms, normally referring to those that have one CH_2 between the double bonds
- Highly unsaturated fatty acids (HUFAs): polyunsaturated fatty acids with three or more double bonds

1.3.3 Position of first double bond (Twining et al., 2016)

- Omega-3 fatty acids: fatty acids with the first double bond on the third carbon atom from the methyl terminus of the carbon chain
- Omega-6 fatty acids: fatty acids with the first double bond on the sixth carbon atom from the methyl terminus of the carbon chain

1.4 Polyunsaturated fatty acids

They have multiple double bonds. The first bond is usually on the third (ω-3) or sixth (ω-6) carbon from the carboxylic tail (Chatterjea and Shinde, 2011)

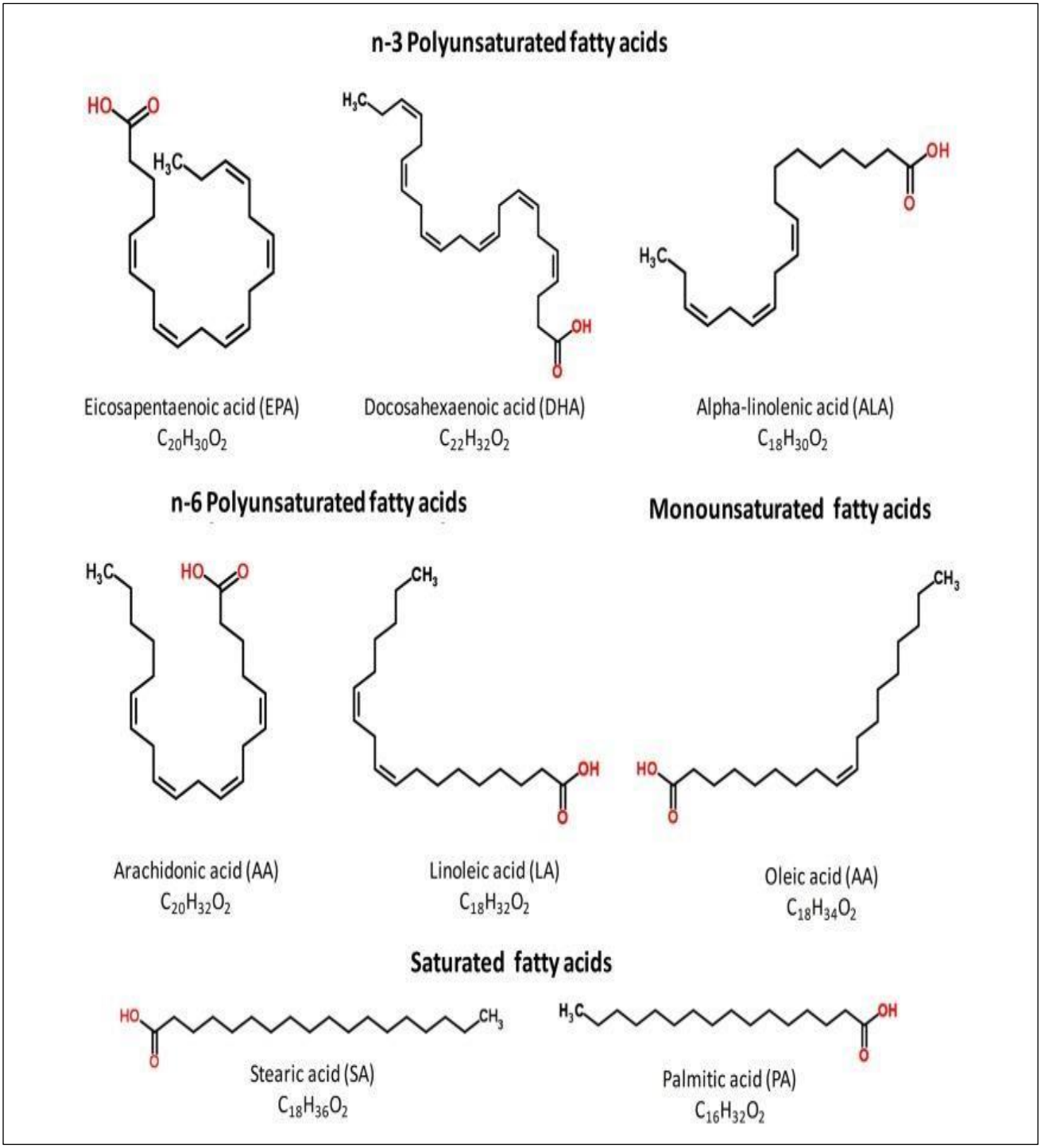

Fig 3. Structure of the main n− 3 (EPA, DHA, and ALA), n− 6 (AA and LA), monounsaturated (OA), and saturated (SA and PA)(Moreno et al., 2012).

Chapter two: Literature Review

2.1 Omega 3

Omega-3 fatty acids are a subset of polyunsaturated Each fatty acid molecule has two ends: the methyl end (or omega end) and the carboxyl end (or alpha end). Major omega-3 fatty acids include alpha-linolenic acid (ALA, C18:3), eicosapentaenoic acid (EPA C20:5), and docosahexaenoic acid (DHA C22:6), Interest in omega-3 (ω-3) polyunsaturated fatty acids (PUFAs) has escalated in recent years because of their various roles in health promotion and disease risk reduction(Shahidi and Ambigaipalan, 2018)

2.2 Type omega-3

- **Linolenic acid series (18:3; 9, 12, 15):** It contains three double Their general formula is $C_{18}H_{32}O_2$
- **Eicosapentaenoic acid (20:5; 5, 8, 11, 14, 17):** It contains five double bonds Their general formula is $C_{20}H_{30}O_2$
- **Docosahexaenoic acid (22:6; 4, 7, 10, 13, 16, 19):** It contains six double bonds Their general formula is $C_{22}H_{32}O_2$

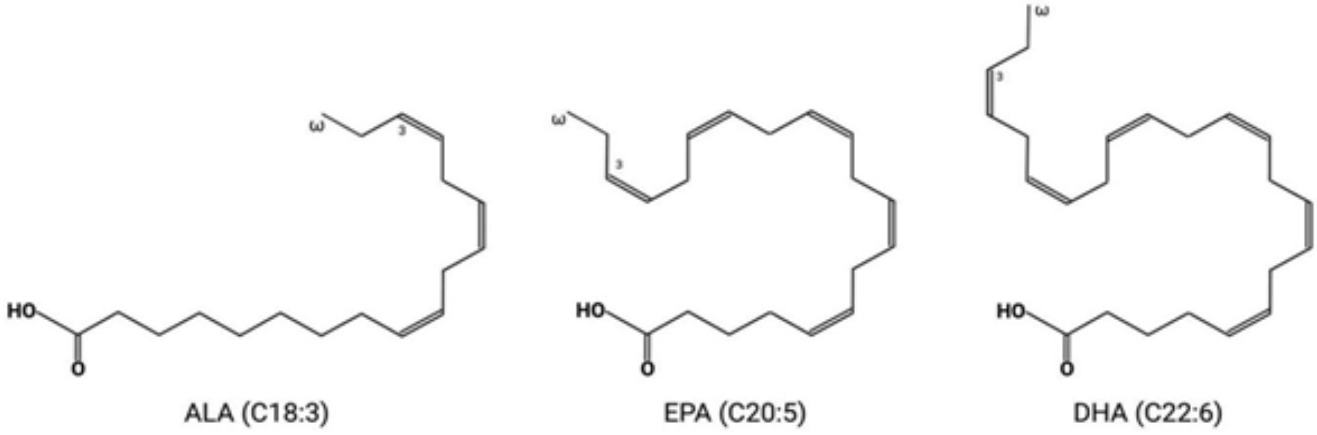

Fig 4. The molecular structure of three major omega-3 fatty acids: alpha-linolenic acid (ALA, C18:3),eicosapentaenoic acid (EPA, C20:5), and docosahexaenoic acid (DHA, C22:6).

2.3 Metabolism omega 3

Fatty acids carry out many functions that are necessary for normal physiological health. Saturated fatty acids are non-essential fatty acids and are harmful if ingested excessively in food. They favor excess weight, insulin resistance, increased LDL cholesterol and are atherogenic. On the contrary, Polyunsaturated fatty acids, have a beneficial effect upon cholesterol metabolism and a protective role against cardiovascular diseases. Long-chain omega-3 fatty acids belong to a family of polyunsaturated fatty acids that are known to have important beneficial effects on metabolism and inflammation. Such effects may confer a benefit in specific chronic noncommunicable diseases. DHA is especially important in the development of the brain, and retina, and Alzheimer's disease (Zamaria, 2004).

Omega 3 fatty acids are one of the important fats that our body needs for various processes but cannot make from scratch. Our body gets omega 3 fatty acids from different types of foods. Omega 3 fatty acids are broadly distributed in nature. Omega 3 fatty acids play a vital role in the human diet and in human physiology (DeFilippis and Sperling, 2006). The unique chemical structure of long carbon chains and multiple double bonds gives omega-3 fatty acids, especially the EPA and DHA, distinctive properties that may lead to significant health benefits. influence the rate of oxidation and signal transduction pathway, and decrease cholesterol accumulation in the cell membrane. omega-3 fatty acids are primarily found in the central nervous system, testes, heart, retina, and immune system .shown that EPA and DHA can affect melatonin, a hormone crucial for sleep regulation.

Furthermore, evidence exists that both EPA and DHA can treat and even prevent anxiety and depression in adults. Therefore, the evidence strongly supports the idea that an increased intake of EPA and DHA can enhance both nervous and mental health.

Omega-3 fatty acid metabolism. The end products of the omega-3 pathway include eicosanoids of the 3 and 5 series, which are anti-inflammatory, inhibit cytokine production, and directly counteract the effect of 2 and 4 series eicosanoids show figure(4) (Patel, 2016)

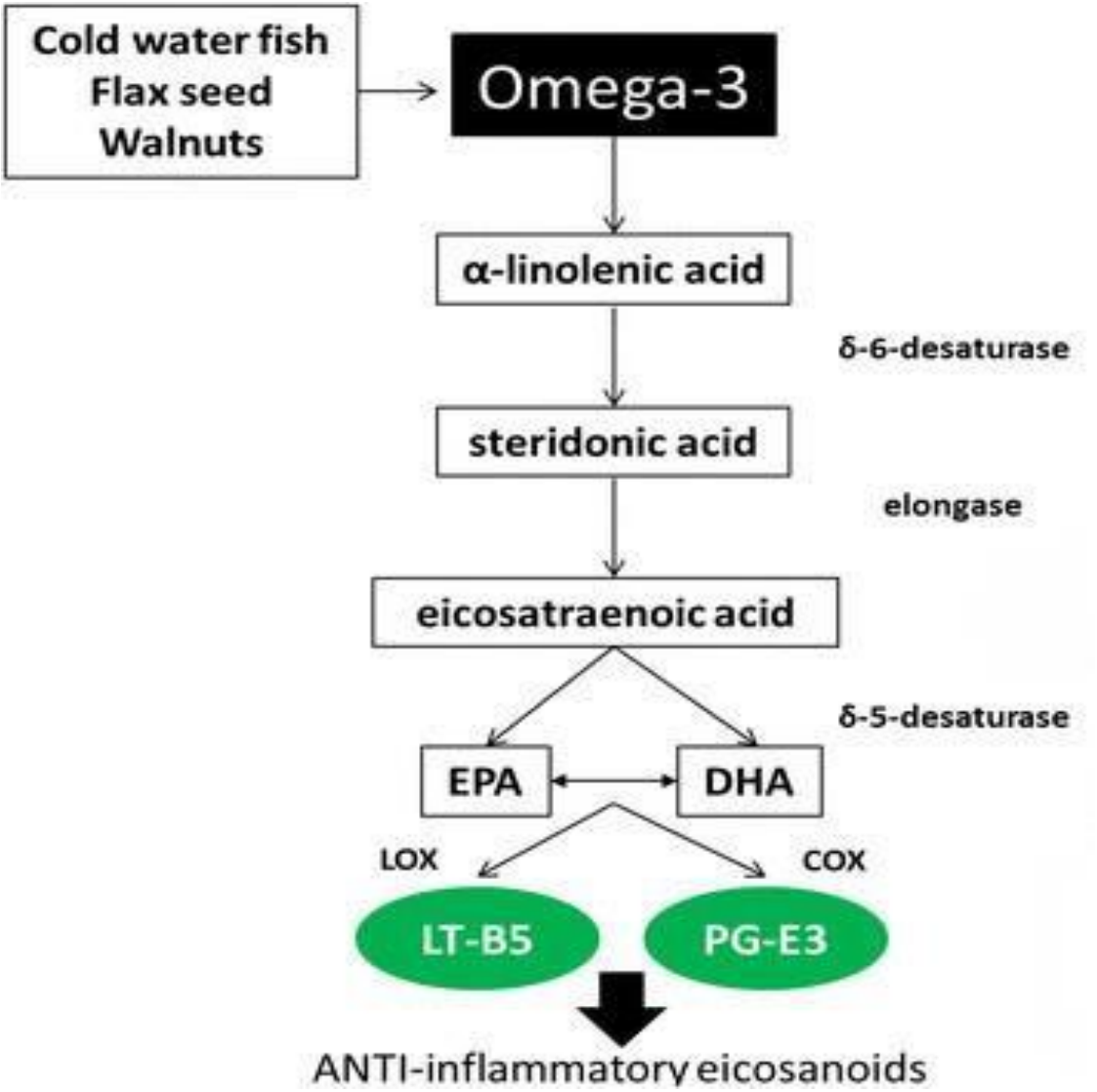

Fig 5. Metabolic pathway omega-3

2.4 SOURCES OF OMEGA-3

ω-3 PUFAs are exclusively found in aquatic organisms and mainly originate in the liver of lean white fish such as cod and halibut, the body of oily fish such as mackerel, menhaden, and salmon, and the blubber of marine mammals such as seals and whales (Shahidi, 1998). The major ω-3 PUFAs from marine sources are EPA and DHA, and DPA is present in fairly low levels in most fish oils.

The primary source of ALA is plants, concentrated mainly in some seeds and nuts and in some vegetable oils (Joint, 2010). Flaxseed, chia seeds, walnut, and echium seed oils are known to be good sources of ALA (Figure2) (Can, 2013), Flaxseed oil contains a high amount of ALA (49.2 g/100 g) and other sources of ALA are walnut, canola, and soybean oils, whereas salmon, sardine, and herring oils contain relatively high amounts of EPA and DHA (Can, 2013).

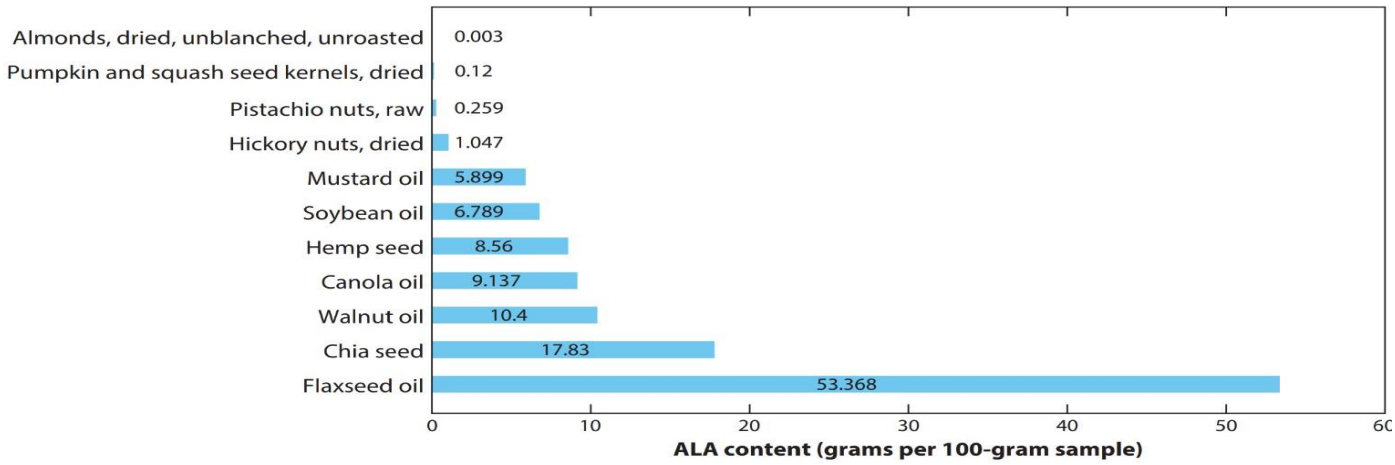

Fig 6. α-Linolenic acid (ALA) content of nuts and seeds(Shahidi and Ambigaipalan, 2018)

EPA and DHA can be synthesized in the human body using ALA as a precursor. However, bioconversion of ALA to EPA and DHA is limited; thus, we require adequate dietary intake of LC ω-3s. Marine oils are also rich sources of fat-soluble vitamins.

Among all fish oils, cod flesh, halibut, and skipjack tuna have been shown to contain the highest amounts of DHA (30% of total FAs), whereas cod flesh, flounder species, and haddock contain the highest amounts of EPA (15–19% of total FAs) (Table 1) (Shahidi and Miraliakbari, 2006). In addition to fish and marine mammals, crustaceans, bivalves, and cephalopods also contain ω-3 PUFA (Table 1).

Marine sources	EPA (%)	DHA (%)	Reference
Fish			
Menhaden oil	18.3	9.6	Ackman 2005
Herring oil	7.5	6.8	
Cod liver oil	12.2	12.7	Copeman & Parrish 2004
Cod flesh oil	19.1	32.6	
Capelin oil	9.3	4.1	
Skipjack tuna oil	11.1	29.1	Tanabe et al. 1999
Butterfish oil	5.1	10.8	Budge et al. 2002
Yellowtail flounder oil	15	18.7	
Winter flounder oil	14.4	20.1	
Haddock oil	14.8	24.8	
Halibut oil	9.6	30.6	
Mackerel oil	8	19.3	
Salmon oil	6.2	9.1	Aursand et al. 1994
Marine mammals			
Bearded seal oil	9.27	13.38	Shahidi 1998
Grey seal oil	5.23	7.12	
Harbor seal oil	9.31	7.76	
Harp seal oil	6.41	7.58	
Hooded seal oil	4.29	7.47	
Ringed seal oil	10.57	26.19	
Crustaceans			
Shrimp	15.26	11.37	Budge et al. 2002
Red crab	12.13	11.93	
Rock crab	20.74	10.35	
Lobster	17.04	7.69	
Bivalves			
Surf clam	22.9	14.3	Copeman & Parrish 2004
Greenland cockle	22.6	16.5	
Blue mussel	19.6	13.2	
Icelandic scallop	26.9	25.9	
Cephalopods			
Common octopus	16.1	20.6	Arts et al. 2001
European squid	14.3	31.6	
Squid	13.9	16.9	

Table 1. Omega-3 polyunsaturated fatty acid content of marine sources(Shahidi and Ambigaipalan, 2018).

Chapter three

3.1 Alzheimer's disease

Alzheimer’s disease is a neurological condition in which the death of brain cells causes a decline in thinking skills and memory. There is currently no cure, but there are ways to support a person through medication and other strategies. The symptoms are mild at first and become more severe over time (Seunggu Han, 2024).

It is named after Dr. Alois Alzheimer, who first described the condition in 1906 Trusted Source. Common symptoms of Alzheimer’s disease include memory loss, language problems, and impulsive or unpredictable behavior. One of the main features of the condition is the presence of plaques and tangles in the brain. Another feature is a loss of connection between the nerve cells, or neurons, in the brain. These features mean that information cannot pass easily between different areas of the brain or between the brain and the muscles or organs. As the symptoms worsen, it becomes harder for people to remember recent events, to reason, and to recognize people they know (Seunggu Han, 2024).

Eventually, a person with Alzheimer’s disease may need full-time assistance. According to the National Institute on Aging, Alzheimer’s disease is the sixth leading cause of death Trusted Source in the U.S. However, other recent estimates suggest that it may be the third Trusted Source leading cause of death, just behind heart disease and cancer (Seunggu Han, 2024).

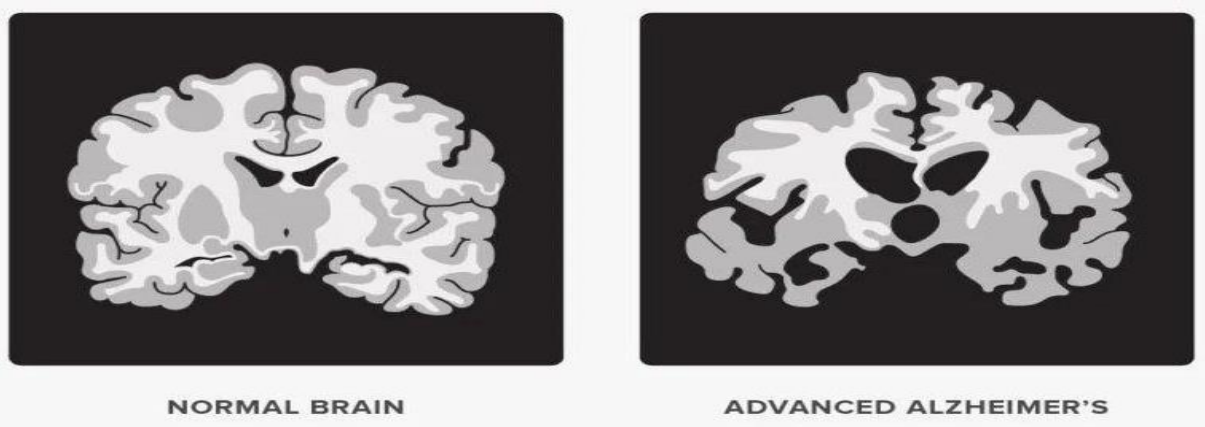

Fig 7. Normal brain vs Advanced Alzheimer’s (Seunggu Han, 2024).

3.2 Symptoms

Alzheimer's disease is a progressive condition, meaning that the symptoms get worse over time. Memory loss is a key feature, and this tends to be one of the first symptoms to develop. The symptoms appear gradually, over months or years. If they develop over hours or days, a person may require medical attention, as this could indicate a stroke (Seunggu Han, 2024)

3.3 Symptoms of Alzheimer's disease include

3.3.1 A. Memory loss: A person may have difficulty taking in new information and remembering information. This can lead to (Seunggu Han, 2024).

- repeating questions or conversations
- losing objects
- forgetting about events or appointments
- wandering or getting lost

3.3.2 B. Cognitive deficits: A person may experience difficulty with reasoning, complex tasks, and judgment. This can lead to (Seunggu Han, 2024).

- a reduced understanding of safety and risks
- difficulty with money or paying bills
- difficulty making decisions
- difficulty completing tasks that have several stages, such as getting dressed

3.3.3 C. Problems with recognition: A person may become less able to recognize faces or objects or less able to use basic tools. These issues are not due to problems with eyesight (Seunggu Han, 2024)

3.3.4 D. Personality or behavior changes: A person may experience changes in personality and behavior that include (Seunggu Han, 2024).

- becoming upset, angry, or worried more often than before
- a loss of interest in or motivation for activities they usually enjoy
- a loss of empathy
- compulsive, obsessive, or socially inappropriate behavior

3.4 Risk factors

3.4.1 Unavoidable risk factors for Alzheimer's disease include (Seunggu Han, 2024).

- aging
- having a family history of Alzheimer's disease
- carrying certain genes

Other factors that increase the risk of Alzheimer's include Trusted Source severe or repeated traumatic brain injuries and having exposure to some environmental contaminants, such as toxic metals, pesticides, and industrial chemicals(Seunggu Han, 2024).

3.4.2 Modifiable factors that may help prevent Alzheimer's include(Seunggu Han, 2024).

- getting regular exercise
- following a varied and healthful diet
- maintaining a healthy cardiovascular system
- managing the risk of cardiovascular disease, diabetes, obesity, and high blood pressure
- keeping the brain active throughout life

3.5 Effect omega 3 on Alzheimer's

Several epidemiological studies have shown that lower intakes of ω-3 PUFAs are associated with an increased risk of cognitive decline or dementia, especially for Alzheimer's disease (Cole et al., 2009). (MacLean et al., 2004) reported that sufficient clinical evidence exists for ω-3s and prevention of Alzheimer's disease. DHA is the primary component of membrane PLs in the brain, especially in the cerebral cortex, mitochondria, (Connor, 2000).

Several reviews have also analyzed the effects of ω-3s on dementia(Cole et al., 2009), (Cunnane et al., 2009). The action mechanism of PUFAs on brain function includes modifications to (a) membrane fluidity, (b) the activity of membranebound enzymes, (c) the number and affinity of receptors, (d) the function of ion channels, (e) the production and activity of neurotransmitters, and (f) signal transduction, which controls the activity of neurotransmitters and neuronal growth fac tors (Yehuda et al., 2005).

(Dijck-Brouwer et al., 2005) investigated umbilical artery and umbilical vein FA compositions as well as early neonatal neuro logical conditions in 317 term infants and reported that lower fetal DHA, AA, and essential FA levels negatively influence the neurological condition of early postnatal neurological condition. Several studies have shown that deficiency in essential FAs, especially ω-3 PUFAs, contributes to attention deficit hyperactivity disorder (ADHD) (Farooqui and Horrocks, 2001), (Ross et al., 2003). found that administration of ω-3 PUFAs significantly improved quality of life, ability to concentrate, sleep quality, and hemoglobin levels in iron-deficient and sleep disturbed attention deficit hyperactivity disorder (ADHD) children.

Overall, the intake of fish and ω-3 PUFAs has been shown to exert a positive cognitive health effect in older healthy adults, whereas consumption of ω-3 PUFAs appears to be controversial when considering patients with Alzheimer's disease (Cederholm, 2017). Cederholm (2017) reported that ω-3 supplementation could also benefit older adults with memory complaints/mild cognitive impairment and Alzheimer's disease based on studies published during 2015– 2016. A summary of clinical studies on the effects of ω-3s in Alzheimer's disease dementia is provided in Table 2.

Findings	Number of persons	Number of incidents	Reference
Intake of phosphatidylserine enriched with DHA (100 mg/day) could improve or maintain cognitive status in elderly subjects with memory complaints	122 elderly individuals	ND	Vakhapova et al. 2014
Low levels of red-blood-cell DHA were associated with smaller brain volumes and a vascular pattern of cognitive impairment even in persons free of clinical dementia	1,575 participants (854 women) aged 67 ± 9 years	ND	Tan et al. 2012b
Increased DHA intake from marine sources reduced the risk of dementia	266 participants	42 dementia and 30 AD	Lopez et al. 2011
Supplementation with algal DHA (2 g/day) did not slow down the rate of cognitive and functional decline in patients with mild to moderate AD	295 individuals with mild to moderate AD	ND	Quinn et al. 2010
The cognitive function did not decline over 2 years of study in healthy adults with administration of 200 mg EPA plus 500 mg DHA	748 cognitively healthy adults (55% men), aged 70–79 years	ND	Dangour et al. 2010
Intake of ω-3 PUFAs was not associated with dementia or AD in the Canadian Study of Health and Aging	663 nondemented subjects aged more than 65 years	149 were incident cases of dementia, including 105 with AD	Kröger et al. 2009
Supplementation with DHA (800 mg/day) and lutein (12 mg/day) significantly improved verbal fluency scores, memory scores, and rate of learning in elderly women	49 women (aged 60–80 years)	ND	Johnson et al. 2008
High consumption of fish (nonprocessed lean fish and fatty fish) and fish products (>10 g/day) was associated with better cognitive performance in a dose-dependent manner in elderly people	2,031 subjects (55% women) aged 70–74 years	80 poor cognitive performance who had low fish consumption (<10 g/day)	Nurk et al. 2007
Intake of fatty fish and marine ω-3 PUFAs reduced the risk of impaired cognitive function in this middle-aged population, whereas intake of cholesterol and saturated fat showed an increased risk	1,613 subjects ranging from 45 to 70 years	ND	Kalmijn et al. 2004
Intake of dietary ω-3 (DHA) PUFAs and fish reduced the risk of incident AD, but EPA did not show any significant effect	815 residents (65 to 94 years), who were initially unaffected by AD	131 participants developed AD	Morris et al. 2003
Consumption of fish (weekly) reduced the risk of AD	8,085 nondemented participants aged 65	281 incident cases of dementia, including 183 AD	Barberger-Gateau et al. 2002

Table 2. Summary of research findings on omega-3s (ω-3) and dementia/Alzheimer's disease (Shahidi and Ambigaipalan, 2018)

Chapter four

4.1 Conclusion

The effectiveness of omega-3 fatty acids in Alzheimer's disease is still a topic of ongoing research. Some studies suggest that omega-3 fatty acids, found in fish oil, may have potential benefits in reducing the risk or slowing the progression of Alzheimer's disease due to their anti-inflammatory and neuroprotective properties. However, more rigorous clinical trials are needed to fully understand the extent of their impact on Alzheimer's disease. Additionally, focusing on a balanced diet rich in omega-3 fatty acids from sources such as fatty fish, nuts, and seeds, as part of a comprehensive approach to brain health, remains prudent. It's always best to consult with a healthcare professional for personalized advice and recommendations.

4.2 Recommendations

the results of studies show the effectiveness of using omega-3, To potentially support brain health and Omega-3's impact on Alzheimer's, consider the following:

1. **Include Fatty Fish in Your Diet:** Eat fish rich in omega-3 fatty acids, such as salmon, mackerel, and sardines, at least twice a week.

2. **opt for Plant-Based Sources:** Incorporate plant-based omega-3 sources like flaxseeds, chia seeds, walnuts, and hemp seeds into your meals.

3. **Consider Omega-3 Supplements:** Consult with your healthcare provider before taking omega-3 supplements to ensure they are appropriate for your individual health needs.

4. **Engage in Regular Exercise:** Incorporate exercise into your routine, as it has been linked to improved cognitive function.

5. **Stay Mentally Active:** Keep your brain engaged with activities like puzzles, reading, and learning new skills.

6. **Prioritize Adequate Sleep:** Ensure you get enough quality sleep, as it plays a crucial role in overall cognitive health.

Remember, these recommendations are part of a broader approach to promoting brain health, and individual responses may vary. Always consult with healthcare professionals for personalized advice based on your specific health conditions.

References

BOUDRAULT, C., BAZINET, R. P. & MA, D. W. 2009. Experimental models and mechanisms underlying the protective effects of n-3 polyunsaturated fatty acids in Alzheimer's disease. *The Journal of nutritional biochemistry,* 20**,** 1-10.

CAN, D. 2013. Food Sources of Omega-3 Fats. *Toronto, Ont.Dietit.*

CEDERHOLM, T. 2017. Fish consumption and omega-3 fatty acid supplementation for prevention or treatment of cognitive decline, dementia or Alzheimer's disease in older adults–any news? *Current Opinion in Clinical Nutrition & Metabolic Care,* 20**,** 104-109.

CHATTERJEA, M. & SHINDE, R. 2011. *Textbook of medical biochemistry*, Wife Goes On.

COLE, G. M., MA, Q.-L. & FRAUTSCHY, S. A. 2009. Omega-3 fatty acids and dementia. *Prostaglandins, Leukotrienes and Essential fatty acids,* 81**,** 213-221.

CONNOR, W. E. 2000. Importance of n− 3 fatty acids in health and disease. *The American journal of clinical nutrition,* 71**,** 171S-175S.

CUNNANE, S. C., PLOURDE, M., PIFFERI, F., BÉGIN, M., FÉART, C. & BARBERGER-GATEAU, P. 2009. Fish, docosahexaenoic acid and Alzheimer's disease. *Progress in lipid research,* 48**,** 239-256.

DEFILIPPIS, A. P. & SPERLING, L. S. 2006. Understanding omega-3's. *American heart journal,* 151**,** 564-570.

DIJCK-BROUWER, D. J., HADDERS-ALGRA, M., BOUWSTRA, H., DECSI, T., BOEHM, G., MARTINI, I. A., BOERSMA, E. R. & MUSKIET, F. A. 2005. Lower fetal status of docosahexaenoic acid, arachidonic acid and essential fatty acids is associated with less favorable neonatal neurological condition. *Prostaglandins, leukotrienes and essential fatty acids,* 72**,** 21-28.

DOC. RNDR. JIŘÍ DOSTÁL, C. 2014. *ESSENTIALS OF MEDICAL CHEMISTRY AND BIOCHEMISTRY,* brno.

DYALL, S. C. 2015. Long-chain omega-3 fatty acids and the brain: a review of the independent and shared effects of EPA, DPA and DHA. *Frontiers in aging neuroscience,* 7**,** 52.

FAROOQUI, A. A. & HORROCKS, L. A. 2001. Plasmalogens, phospholipase A 2, and docosahexaenoic acid turnover in brain tissue. *Journal of Molecular Neuroscience,* 16**,** 263-272.

JOINT, F. 2010. Fats and fatty acids in human nutrition. Report of an expert consultation, 10-14 November 2008, Geneva.

MACLEAN, C. H., MOJICA, W. A., MORTON, S. C., PENCHARZ, J., GARLAND, R. H., TU, W., NEWBERRY, S. J., JUNGVIG, L. K., GROSSMAN, J. & KHANNA, P. 2004. Effects of omega-3 fatty acids on lipids and glycemic control in type II diabetes and the metabolic syndrome and on inflammatory bowel disease, rheumatoid arthritis, renal disease, systemic lupus erythematosus, and osteoporosis: Summary. *AHRQ evidence report summaries.* Agency for Healthcare Research and Quality (US).

MORENO, C., MACÍAS, Á., PRIETO, Á., DE LA CRUZ, A., GONZÁLEZ, T. & VALENZUELA, C. 2012. Effects of n− 3 polyunsaturated fatty acids on cardiac ion channels. *Frontiers in physiology,* 3**,** 25629.

MORRIS, M. C., BROCKMAN, J., SCHNEIDER, J. A., WANG, Y., BENNETT, D. A., TANGNEY, C. C. & VAN DE REST, O. 2016. Association of seafood consumption, brain mercury level, and APOE ε4 status with brain neuropathology in older adults. *Jama,* 315**,** 489-497.

PATEL, J. A. K. V. A. B. D. A. K. M. A. M. R. A. A. K. 2016. OrganSpecific Nutrition: One for the History Books or Still an Active Player? *current Surgery Reports,* 4.

PURI, D. 2011. *Textbook of Medical Biochemistry,* india, Elseviar.

ROSS, B. M., MCKENZIE, I., GLEN, I. & BENNETT, C. P. W. 2003. Increased levels of ethane, a non-invasive marker of n-3 fatty acid oxidation, in breath of children with attention deficit hyperactivity disorder. *Nutritional neuroscience,* 6**,** 277-281.

RUSTAN, A. C. & DREVON, C. A. 2001. Fatty acids: structures and properties. *e LS.*

SCHAEFER, E. J., BONGARD, V., BEISER, A. S., LAMON-FAVA, S., ROBINS, S. J., AU, R., TUCKER, K. L., KYLE, D. J., WILSON, P. W. & WOLF, P. A. 2006. Plasma phosphatidylcholine docosahexaenoic acid content and risk of dementia and Alzheimer disease: the Framingham Heart Study. *Archives of neurology,* 63**,** 1545-1550.

SEUNGGU HAN, M. D. 2024. Medically reviewed *Markus MacGill*
SHAHIDI, F. 1998. Functional seafood lipids and proteins. *Functional Foods***,** 381-98.

SHAHIDI, F. & AMBIGAIPALAN, P. 2018. Omega-3 polyunsaturated fatty acids and their health benefits. *Annual review of food science and technology,* 9**,** 345-381.

SHAHIDI, F. & MIRALIAKBARI, H. 2006. Marine oils: compositional characteristics and health effects. *Nutraceutical and Specialty Lipids and their Co-products.* CRC Press

SINGER, P. & RICHTER-HEINRICH, E. 1991. Stress and fatty liver—possible indications for dietary long-chain n-3 fatty acids. *Medical hypotheses,* 36**,** 90-94.

TWINING, C. W., BRENNA, J. T., HAIRSTON JR, N. G. & FLECKER, A. S. 2016. Highly unsaturated fatty acids in nature: what we know and what we need to learn. *Oikos,* 125**,** 749-760.

YEHUDA, S., RABINOVITZ, S. & MOSTOFSKY, D. 2005. Essential fatty acids and the brain: from infancy to aging. *Neurobiology of aging,* 26**,** 98-102.

ZAMARIA, N. 2004. Alteration of polyunsaturated fatty acid status and metabolism in health and disease. *Reproduction Nutrition Development,* 44**,** 273-282.