

**Biomedical Journal of Indonesia** 

Journal Homepage: <u>https://www.jurnalkedokteranunsri.id/index.php/BJI/index</u>



# Omega-3 as an Anti-Inflammatory Modality: Literature Review

#### Rachmat Hidayat<sup>1\*</sup>, Nur Riviati<sup>2</sup>

<sup>1</sup>Department of Biology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia <sup>2</sup>Department of Internal Medicine, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

## ARTICLE INFO

**Keywords:** Omega-3 Saturated fat Inflammation

\*Corresponding author: Rachmat Hidayat

E-mail address:

dr.rachmat.hidayat@gmail.com

All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.32539/BJI.v7i1.12

## 1. Introduction

These omega-3 fatty acids are derived from their precursors, namely linoleic and linolenic essential fatty acids. Essential fatty acids cannot be formed in the body and must be supplied directly from food.<sup>1-4</sup> Then the precursors enter the elongate and desaturate processes which produce three forms of omega-3 fatty acids: LNA (alpha-linolenic acid (C 18: 3, n -3)), EPA (eicosapentaenoate (C20: 5, n- 3)), and DHA (docosahexaenoate (C22: 6, n-3).<sup>5-8</sup>

The parent of omega-3 fatty acids is alpha linolenic acid (ALA). ALA with the help of the delta-6-desaturase enzyme can be converted into stearidonic acid, then by the delta-5-desaturase enzyme the body is converted to eicosapentaenoic acid (EPA) and by the delta4desaturase enzyme it is converted to docosahexaenoic acid (DHA).<sup>9-10</sup> The process of making DHA and AA facilitated by the enzymes desaturase and elongase. The activity of these two enzymes is still lacking in premature infants, even in term infants up to the age

### ABSTRACT

Omega-3 fatty acids are polyunsaturated fatty acids that have multiple double bonds, the first double bond is located on the third carbon atom of the omega-methyl group, the next double bond is located at the third carbon atom from the previous double bond. The methyl omega group is the last group in the fatty acid chain. Omega-3 fatty acids are nutrients that play a vital role in the growth and development process of brain neuron cells for the intelligence of the born baby.

of 4-6 months. Therefore, the addition of DHA and AA in premature infants is highly recommended at a dose that refers to the fatty acid content in breast milk.<sup>11</sup>

The activity of both desaturase and elongase enzymes is influenced by the fatty acids found in food. Fish oil that contains a lot of DHA will inhibit the activity of this enzyme so that it can inhibit the formation of AA.<sup>12</sup> In contrast, corn oil or saf-flower stimulates the activity of the desaturase enzyme, thereby increasing the formation of AA1. The physical and chemical properties of the metabolism, digestion, absorption and secretion of omega-3s are the same as those of fat.<sup>13-15</sup>

The physical properties of triglycerides are determined by the proportion and chemical structure of the fatty acids that make up them. The more shortchain fatty acids and unsaturated bonds there are, the softer and more fluid the fats are. Preferably, the more long-chain saturated fatty acids, such as plammic acid (CI 6: 0) and stearic acid (18: 0) that are found in animal fat, the denser the fat. Triglyceride properties are also determined by the position (omega) and the position of fatty acids on the glycerol molecule.<sup>16,17</sup>

#### Classification, source of omega-3 and nomenclature

Fatty acids are distinguished according to the number of carbon they contain, namely short chain fatty acids (6 carbon atoms or less), medium chain (8 to 12 carbon), long chain (14 - 18 carbon), and very long chain (20 carbon atoms or more).<sup>18</sup> Essential fatty acids actually consist of linoleic acid (AL) / "linoleic acid" (LA), linolenic acid (ALN) / "- linolenic acid" (ALA) and arachidonic acid / "arachidonic acid" (AA), fatty acids it cannot be made by the body either from other fatty acids. Arachidonic acid can be made from linolenic acid (n-6 series), therefore only linolenic fatty acids and linoleic fatty acids are considered as essential fatty acids.

These two essential fatty acids cannot change from one another and differ both in metabolism and function, even physiologically they both have opposite functions, contain one double bond, whereas polyunsaturated fatty acids contain two or more double bonds. . The classification of fatty acids according to the length of the carbon chain and the level of saturation in fat which is abundant in nature can be seen in table 2.3.<sup>22</sup>

Sources of omega-3 fatty acids and the amount of omega 3 content in food, namely: Mackerel (2.5 gr); Herring (1.7 gr); Salmon (1.2 gr) Crustacean / lobster (0.2 gr); Squid (0.6 gr); Salmon oil (19.9 gr); Cod liver oil (18.5 gr); Herring oil (11.4 gr). The need for omega-3 fats will produce fatty acids and cholesterol which are actually needed to form membrane cells in all organs. Important organs such as the retina and central nervous system are mainly composed of fat. Fatty acids that are needed by body tissues, especially essential fatty acids. Essential fatty acids are fatty acids that cannot be made in the body so they must be obtained from food, consisting of linoleic, linolenic and arachidonic acids.<sup>23-26</sup>

Fatty acids consisting of carbon chains that hold all of the hydrogens that can be bound are called saturated fatty acids. Fatty acids that contain one or more double bonds to which a hydrogen atom can be added are called unsaturated fatty acids. WHO (1990) recommends that fat consumption as much as 15-30% of total energy needs is considered good for health. This amount meets the need for essential fatty acids and to aid in the absorption of fat-soluble vitamins.<sup>27-30</sup>

Among the fats consumed in a day, it is recommended that at most 10% of total energy needs come from saturated fat, and 3-7% from polyunsaturated fat. The recommended cholesterol intake is <300 mg daily. The recommendations given by the FAO / WHO expert group regarding the consumption of saturated fatty acids, unsaturated fatty acids and cholesterol are: (1) the consumption of saturated fatty acids should not exceed 10% of the total energy (2) It is recommended that the consumption of linoleic fat contributes between 4-10 % of total energy. Consumption higher than this range is recommended if the consumption of saturated fat and high cholesterol, and (3) the consumption of cholesterol from food is recommended to be less than 300 mg / day.<sup>31-</sup> 32

WHO has set recommendations regarding the intake of omega 3 for each person, namely 0.3 -0.5 g / day (EPA + DHA). Which includes unsaturated fatty acids are: omega-3 (EPA & DHA), omega-6, AA, omega-9. Essential fatty acids are especially important for normal growth and development of fetuses and babies, as well as for brain development and vision.<sup>33</sup>

#### **Benefits of Omega-3**

The advantage of omega-3 is very important for health, even most important among other fatty acids because it has anti-inflammatory and anti-clotting effects, is also good for the central nervous system and brain and can prevent CVD. The most abundant omega-3 fatty acids in fish are EPA and DHA. Consuming fish regularly can prevent CVD. Omega-3 unsaturated fatty acids play an important role in the morphological, biochemical, and molecular development of the brain and other organs.<sup>34</sup>

Lack of omega-3 fatty acids, caused by insufficient intake or due to diseases that reduce absorption, can inhibit brain development, physical health and environmental interactions, which have a strong effect on the formation of cognitive development. Prolonged omega-3 deficiency can be fatal. Lack of omega-3 fatty acids causes nerve and vision problems and can interfere with the development of the nervous system. As a result, there may be disturbances in the immune system, memory, mental and vision.<sup>35-36</sup>

Excessive provision of fat can lead to obesity and heart disease and can even lead to malignancy, can increase cholesterol levels, LDL which can spur the occurrence of atherosclerosis and coronary heart disease. This really depends on the amount of energy that comes from fat, the composition of the fatty acids, the composition from lipoproteins, dietary fiber consumed, antioxidants, activity, and degree of health. Saturated fatty acids such as lauric, myristic, and palmitic acid can increase cholesterol levels and LDL levels, while giving polyunsaturated fatty acids can reduce cholesterol and LDL levels. Monounsaturated oleic acids do not increase LDL levels but can increase HDL lipoproteins.<sup>37,38</sup>

Omega-6 and omega-3 fatty acids act as precursors or raw materials for eicosanoid compounds, which are highly reactive compounds. The eicosanoid compounds produced by omega-6 and omega-3 fats are often different, if not opposite. Thus, because omega-6 and omega-3 fatty acids compete as eicosanoid precursors and also have different biological roles, the balance between these two fatty acids in the daily diet is very important.<sup>39</sup>

In premature babies who are underweight (2.500 g) and whose brain size is smaller than average. Because the number of neuron cells is also small, the baby can be deformed, have low quality and the process of brain cell growth and development is not normal or below optimal. Omega-3 fatty acids, EPA are also reported to play a role in preventing degenerative diseases since the fetus and during adulthood.<sup>40</sup>

When the fetus is in the womb, EPA is indispensable in the formation of blood vessel and heart cells. Meanwhile, as an adult, EPA functions to nourish blood, work mechanism of blood vessels and work of sacs that regulate blood circulation. Therefore, due to a deficiency of omega-3 EPA, you can be at risk of suffering from blood vessel and heart disease. The balance of the ratio of EPA, DHA, and AA in the blood of infants, adolescents, or adults can be used as an indicator to predict the risk of vascular system disorders and heart disease in the future.<sup>41</sup> Preventive measures are highly recommended from an early age in order to avoid this degenerative disease. Food supply sources of omega-3, EPA, DHA, AA, and alpha-linolenic acid should be consumed in a balanced ratio. The ratio of consumption of omega 3: omega 6 is 1: 5 to 10:19. DHA is needed as a cup-forming element for the rhodopsin container, namely a vital compound for sensing and sending back signals received by the eye to the brain. *Docosahexaenoic Acid* (DHA) and *Arachidonic Acid* (AA) are nutritional elements which are also important in the growth and development of nerves in the brain and help form brain fat tissue (mylenisation) and maintain the interconnection of brain nerve cells, especially to influence brain development.<sup>42</sup>

DHA and AA are the largest components of longchain polyunsaturated fatty acids (LC-PUFA), which are very important ingredients for the central nervous system organs. DHA is important for the formation of nerve tissue, while AA acts as a neurotransmitter and as an essential form of LC-PUFA fatty acids that must be added to food. Based on the results of research, supplementation of several fatty acids at an early age has shown improvement in the index of mental development and visual acuity but only at levels of 17 mg / 100 kkalDHA and 34 mg / 100 kkalAA.<sup>43</sup>

These levels are almost the same as the FAO / WHO recommendation for infant formula, which is based on average levels of breast milk throughout the world. The adequacy rate of DHA is 20 mg / kg BW / day. According to the POM, consuming excessive DHA and EPA can inhibit the formation of AA from linoleic acid, can suppress the activity of the cyclooxygenase enzyme that forms prostaglandins. Consuming excessive DHA can cause kidney damage as a result, the kidneys experience a decreased response to the inflammatory process so that the inflammation period is longer and there is a decrease in the production of enzymes that play a role in controlling kidney function.<sup>44</sup>

The consequences of consuming excess DHA have not been studied. However, these effects are believed by experts to persist and occur when children become adults. AA and DHA supply is needed, especially in the last trimester, post-birth and early childhood. Deficiency of these two types of essential fatty acids at birth is correlated with low body weight, small head circumference and low placental size as a result of which the development of the central nervous system and later cognitive abilities are affected. DHA deficiency is linked to attention deficit-hyperactivity disorder (ADD or ADHD) such as excessive physical activity, learning difficulties and lack of social skills.<sup>44</sup>

General Nomenclature	Chemical term	Short Nomenclature	Source
Polyunsaturated Omega - 3 Linoleic **	Acid 9.12.15 - Octnearrieonic	18:3(n-3/w-3)	Soybean oil, sprouts, wheat
Eicosapentaenoate / EPA	5,8,11,14,17- Eikosapentaeonic acid	20:5(N-3/w-3)	Certain fish oils (can be made from linoleic acid
Docosahexanoate / DHA	4,7,10,13,16,19 - 22: 6 (N- 3 / w-3) Docosahexanoic acids	22:6(n-3/w-3)	Breast milk, certain fish oil

Table 1. Classification of Omega-3 and sources.

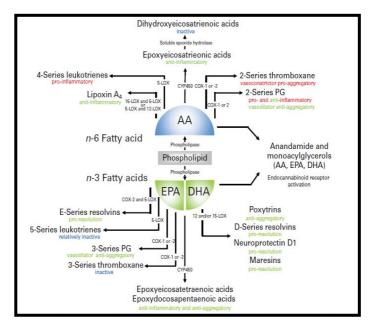


Figure 1. EPA and DHA as anti-inflammatory

# 2. References

- World Health Organization (WHO). Article: World Population Aging 2019: Highlights-The United Nations. 2019. <u>https://www.un.org-villagepublications-pdf.accessed in December 2019</u>
- Indonesian Ministry of Health. Article: Indonesia Entering the Aging Population Period. Thursday, 4 July 2019.

https://www.depkes.go.id/article/view/1907050 0004/indonesia-masuki-periode-agingpopulation.html accessed in December 2019.

 World Health Organization (WHO). Article: Aging and Health. 5 February 2018. https://www.who.int/news-room/factsheets/detail/ageing-and-health accessed on December 2019.

- Trevisan K. "Theories of Aging and the Prevalence of Alzheimer's Disease." BioMed Research International 2019.
- Heymsfield SB. Skeletal muscle mass and quality: evolution of modern measurement concepts in the context of sarcopenia. Proceedings of the Nutrition Society, 2015; 74.4: 355-366.
- Alexandre Tda S, Duarte YA, Santos JL. Sarcopenia according to the European Working Group on Sarcopenia in Older People (EWGSOP)

versus dynapenia as a risk factor for mortality in the elderly. J Nutr Health Aging, 2014; 18:751– 756.

- Ministry of Communication and Information of the Republic of Indonesia (Kominfo). Article: Independent and Prosperous Elderly. 2019. https://kominfo.go.id/index.php/content/detai 1/19022/lansia-mandiri-sejahtera/0/artikelgpr accessed on December 2019
- Abdelhamid A. The relationship between omega-3, omega-6 and total polyunsaturated fat and musculoskeletal health and functional status in adults: a systematic review and meta-analysis of RCTs. Calcified tissue international, 2019, 105.4: 353-372.
- Ethgen O, Beaudart C, Buckinx F, Bruyere O, Reginster JY. The future prevalence of sarcopenia in Europe: a claim for public health action. Calcif Tissue Int, 2016; 100:229–234
- Yazar T, Yazar HO. Prevalance of sarcopenia according to decade. Clinical nutrition ESPEN, 2019, 29: 137-141.
- Skaaby T, Betina HT, Allan L. "Vitamin D, Sarcopenia and Aging." Vitamin D in Clinical Medicine. Vol. 50. Karger Publishers, 2018. 177-188.
- Calvani R "Biomarkers for physical frailty and sarcopenia: state of the science and future developments." Journal of cachexia, sarcopenia and muscle,2015: (6.4) 278-286
- 13. Bianchi L. "Prevalence and clinical correlates of sarcopenia, identified according to the EWGSOP definition and diagnostic algorithm, in hospitalized older people: The GLISTEN Study." Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences, 2017: (72.11) 1575-1581.
- McGlory C, Philip C, Everson AN. "The Influence of Omega-3 Fatty Acids on Skeletal Muscle Protein Turnover in Health and Disease." Frontiers in nutrition 6 2019: (6)144.
- McKee A, John EM. "Hormones and Sarcopenia." Current Opinion in Endocrine and Metabolic Research, 2019.
- Jeromson S, Mackenzie I, Doherty MK, Whitfield PD, Bell G, Dick J. Lipid remodeling and an altered membrane-associated proteome may

drive the differential effects of EPA and DHA treatment on skeletal muscle glucose uptake and protein accretion. Am J Physiol Endocrinol Metab. (2018) 314: E605–19.

- 17. Maddox, George L. The encyclopedia of aging: a comprehensive resource in gerontology and geriatrics. Springer, 2013.
- Peterson SJ, Mozer M. The differentiation between Srcopenia and Cachexia among cancer patient. Nutriotion in clinical practice, 2017, 32(1):30-39.
- Manini TM, Gundermann DM, Clarck BC. Aging of The Muscles and Joints. Hazzard's Geriatric Medicine and Gerontology. 7th edition, Chapter 113, 2017; p.1715-37
- Cruz-Jentoft AJ. "Sarcopenia: revised European consensus on definition and diagnosis." Age and ageing 48.1 (2018): 16-31.
- Ashton-Miller JA, Alexander NB. Biomechanics of Mobility. Hazzard's Geriatric Medicine and Gerontology. 7<sup>th</sup> ed, Chapter 114, 2017; p.1739-53
- Cruz-Jentoft AJ, et al. "Sarcopenia: European consensus on definition and diagnosisReport of the European Working Group on Sarcopenia in Older PeopleA. Age and ageing 39.4, 2010: 412-423.
- Bian A. A study on relationship between elderly sarcopenia and inflammatory factors IL-6 and TNF-a. European journal of medical research, 2017, 22.1: 25.
- Brown JC, Harhay MO, Harhay MN: Sarcopenia and mortality among a population-based sample of community-dwelling older adults. J Cachexia Sarcopenia Muscle 2016;7:290–298.
- 25. Bischoff-Ferrari HA, Willett WC, Orav EJ, Lips P, Meunier PJ, Lyons RA. A pooled analysis of vitamin D dose requirements for fracture prevention. N Engl J Med, 2012;367:40-49
- 26. Dupont J. "The role of omega-3 in the prevention and treatment of sarcopenia." Aging clinical and experimental research, 2019; 1-12.
- 27. Tessier AJ, Chevalier S. An update on protein, leucine, omega-3 fatty acids, and vitamin D in the prevention and treatment of sarcopenia and functional decline. Nutrients, 2018; 10(8), 1099.
- 28. Di Girolamo FG, Situlin R, Mazzucco S, Valentini

R, Toigo G, Biolo G. Omega-3 fatty acids and protein metabolism: enhancement of anabolic interventions for sarcopenia. Current Opinion in Clinical Nutrition & Metabolic Care, 2014; 17(2), 145-150.

- Marzetti E. "The Aging Muscle and Sarcopenia: Interaction with Diet and Nutrition." Molecular Basis of Nutrition and Aging. Academic Press, 2016; p.355-361.
- 30. Witard OC, Emilie C, Stuart RG. "Long-chain n-3 fatty acids as an essential link between musculoskeletal and cardio-metabolic health in older adults." Proceedings of the Nutrition Society, 2019; 1-9.
- Baylis D, Bartlett DB, Patel HP.Understanding how we age: insights into inflammaging. Longev Healthspan, 2013; 2:8
- Bano G, Trevisan C, Carraro S. Inflammation and sarcopenia: a systematic review and metaanalysis. Maturitas, 2017; 96:10–15
- 33. Karstoft K, Pedersen BK. Skeletal muscle as a gene regulatory endocrine organ. Curr Opin Clin Nutr Metab Care, 2016; 19:270–275
- Benatti FB, Pedersen BK. Exercise as an antiinflammatory therapy for rheumatic diseasesmyokine regulation. Nat Rev Rheumatol, 2015; 11:86–97
- 35. Trappe TA, Carroll CC, Dickinson JM. Influence of acetaminophen and ibuprofen on skeletal muscle adaptations to resistance exercise in older adults. Am J Physiol Regul Integr Comp Physiol, 2011; ( 300)R655–R662
- 36. Abdelhamid AS, Brown TJ, Brainard JS et al. Omega-3 fatty acids for the primary and secondary prevention of cardiovascular disease. Cochrane Database Syst Rev 2018. (11) d003177
- 37. Vannice G, Rasmussen H. Position of the

academy of nutrition and dietetics: dietary fatty acids for healthy adults. J Acad Nutr Diet, 2014; 114:136–153

- 38. Papanikolaou Y, Brooks J, Reider C. U.S. adults are not meeting recommended levels for fish and omega-3 fatty acid intake: results of an analysis using observational data from NHANES 2003– 2008. Nutr J, 2014; 13:31
- Sokola-Wysoczanska E, Wysoczanski T, Wagner J. Polyunsaturated fatty acids and their potential therapeutic role in cardiovascular system disorders—a review. Nutrients, 2018; 10:1561
- 40. Kiecolt-Glaser JK, Epel ES, Belury MA. Omega-3 fatty acids, oxidative stress, and leukocyte telomere length: a randomized controlled trial. Brain Behav Immun, 2013; 28:16–24
- 41. Konagai C, Yanagimoto K, Hayamizu K. Effects of krill oil containing n-3 polyunsaturated fatty acids in phospholipid form on human brain function: a randomized controlled trial in healthy elderly volunteers. Clin Interv Aging. 2013; 8:1247–1257
- 42. Dangour AD, Allen E, Elbourne D. Effect of 2-y n-3 long-chain polyunsaturated fatty acid supplementation on cognitive function in older people: a randomized, double-blind, controlled trial. Am J Clin Nutr. 2010; 91:1725–1732
- 43. Gray SR, Mittendorfer B. Fish oil-derived n-3 polyunsaturated fatty acids for the prevention and treatment of sarcopenia. Curr Opin Clin Nutr Metab Care. 2018; 21:104–109
- 44. Smith GI, Atherton P, Reeds DN. Dietary omega-3 fatty acid supplementation increases the rate of muscle protein synthesis in older adults: a randomized controlled trial. Am J Clin Nutr, 2011,93:402–412.