1(3): 142-149 (2015) doi: 10.3153/JFHS15014

Journal of Food and Health Science

E-ISSN 2149-0473

REVIEW ARTICLE DERLEME MAKALESİ

FISH OILS AND HUMAN HEALTH

Eda ÖZER ANDIZ, Mustafa ÜNLÜSAYIN

Department of Seafood Processing Technology, Faculty of Fisheries, Akdeniz University, Campus, Antalya, Turkey

Received: 14.04.2015

Accepted: 21.05.2015

Published online: 04.06.2015

Corresponding author:

Mustafa ÜNLÜSAYIN, Department of Seafood Processing Technology, Faculty of Fisheries, Akdeniz University, Campus, 07059, Antalya, Turkey

E-mail: munlusayin@akdeniz.edu.tr

Abstract:

Fish oils have been essential for human life development, growth and they play critical roles in health and reproduction. Especially of those sources of food which contain adequate levels of polyunsaturated fatty acids (PUFAs) is importantly. On the other hand PUFA's sources of food which have suitable ratios of the n-3 (18-carbon, α-linolenic acid, ALA) to n-6 (18-carbon linoleic acid, LA) PUFAs is more importantly. In recent years, the importance of adequate and well balanced diets have understood and nutritional habits were started to be changing with growing technology. It's known that n-3 and n-6 long chain fatty acids source in especially oily fish had to in our diet in balance. Fish oils play important role prevention of cardiovascular problems, effective for the visual function, brain development and growth. In this review polyunsaturated fatty acids which have an impact on human health were able to be reviewed for this reasons.

Keywords:

Fish oil, Lipids, PUFA, Essential oils, Human health

Introduction

Many of the fatty acids can be synthesized by humans, but there is a group of polyunsaturated fatty acids (PUFAs), the essential fatty acids that the human body cannot produce omega-3 (n-3) and omega-6 (n-6) fatty acids. Omega-3 fatty acids eicosapentaenoic acid (EPA) or docosahexaenoic acid (DHA); however, the data on the shorter-chain omega-3 fatty acid ALA were far less certain (Wang et al., 2004). The major sources of EPA and DHA in food and dietary supplements were found in fatty fish, fish products, marine oils, and certain algae oils. It is influenced not only by the kind of fish but also by the maturity, season, food availability and feeding habit. Fat deposition occurs in muscle tissue (e.g. carp, herring), in liver (cod, haddock, saithe) or in intestines (blue pike, pike, perch). Fish and fish oils contain omega3 (n-3) fatty acids; in particular, EPA (C20:5 x3) and DHA (C22:6 x3) (Holub and Holub, 2004), which is originated from phytoplankton and seaweed in the food chain (Visentainer et al., 2007). The rate of conversion by humans of ALA to EPA is low, with estimates ranging from 0.2% to 15%, as is the conversion of EPA to DHA (Kris-Etherton et al., 2002). However, in two researches have been reported that high intakes of ALA significant increases in long chain omega-3 fatty acids in various body compartments (Francois et al., 2003). Major sources of dietary and supplemental ALA are from soybean and canola oils, walnuts and flax seed (Sontrop and Campbell, 2006).

The parent omega-6 fatty acid is linoleic acid (C18:2 n-6, LA) and the parent omega-3 fatty acid is α-linolenic acid (C18:3 n-3, ALA). Omega-6 fatty acids as arachidonic acid (C20:4n-6; AA) could be synthesized by humans from LA, and omega-3 fatty acids, as eicosapentaenoic acid (C20:5 n-3; EPA), docosapentaenoic acid (C22:5 n-3, DPA) and docosahexaenoic acid (C22:6 n-3, DHA), from ALA; however, the conversion of ALA in EPA, DPA and DHA is low and these omega-3 fatty acids are considered essential fatty acids too. Therefore, both n-3 and n-6 PUFA are entirely derived from the diet and necessary for human health (Rubio-Rodríguez et al., 2010).

Since the conversion of ALA to EPA and DHA are not particularly efficient in humans. Preformed dietary sources of EPA and DHA are the best way to ensure adequate intake; oily fish such as tuna, salmon, mackerel, and sardines are rich in preformed EPA and DHA (McGregor et al., 2001).

Health Effects of Fish Oils

The long chain EPA and DHA could alter cell membrane structure and function by increasing fluidity (Yaqoob and Shaikh, 2010) and n-3 fatty acid (FA) rich particles use direct lipid–lipid proteoglycan interactions for blood clearance and cell uptake (Densupsoontorn et al., 2008, Murray-Taylor et al., 2010). The most noticeable effects come from studies where the substitution of saturated fat with oleic acid has been tested. Isocaloric replacement of about 5% of energy from saturated fatty acids by oleic acid (or PUFA) has been estimated to reduce coronary heart disease risk by 20–40% mainly via low-density lipoprotein (LDL) cholesterol reduction (Kris-Etherton, 1999). The other beneficial effects on risk factors for cardiovascular disease (CVD) such as factors related to thrombogenesis, in vitro LDL oxidative susceptibility and insulin sensitivity have been reported by Kris-Etherton (1999) and Vessby et al., (2001). n-3 PUFAs have the ability to respond to inflammation in atherogenesis through direct and indirect mechanisms. A direct mechanism through which n-3 PUFA decrease inflammation includes its rapid effect on the regulation of transcription factors (Arterburn et. al.,2006) and indirect modes of actions include the production of three- and fiveseries eicosanoids and inflammation-resolving lipid mediators (Adkins and Kelly, 2010).

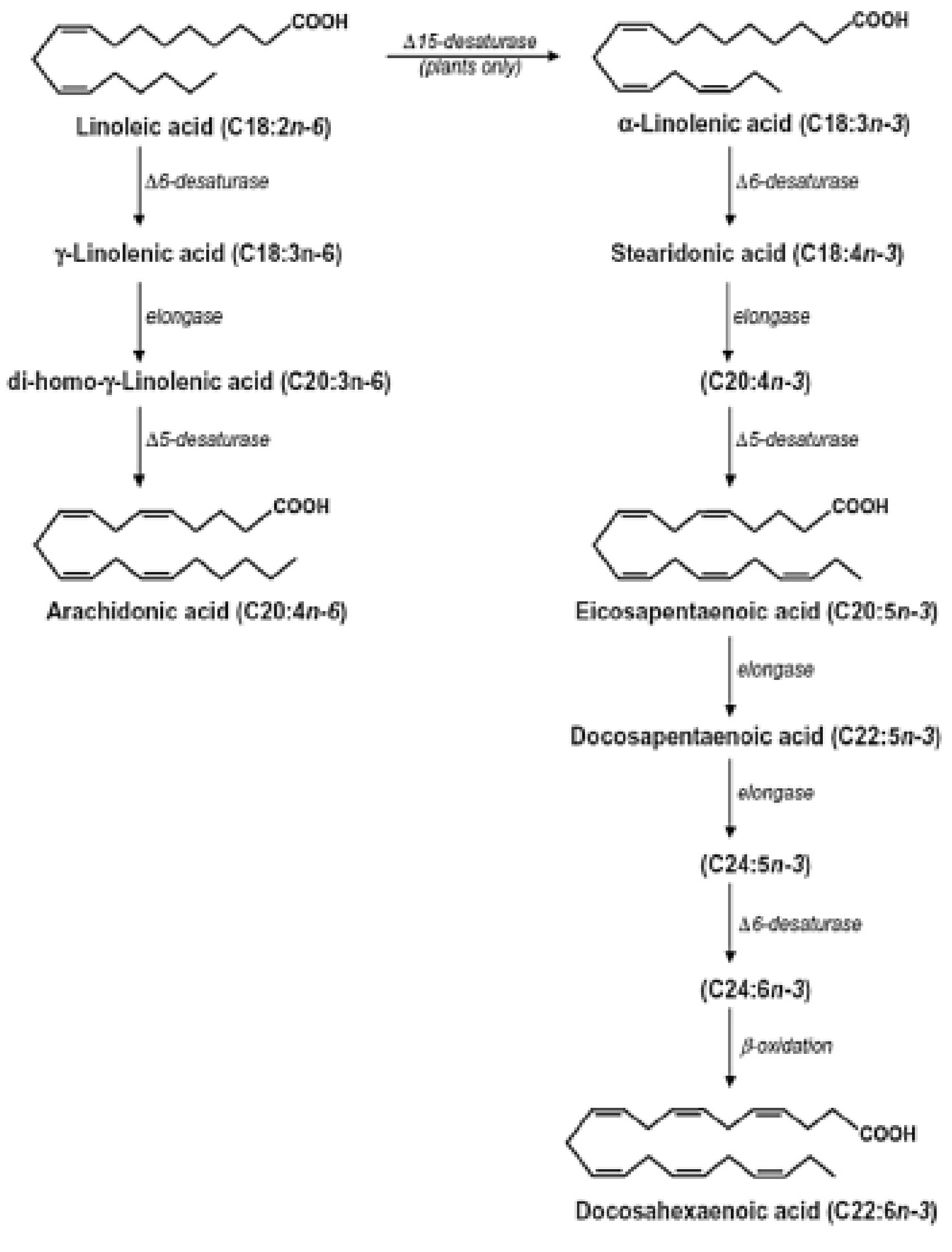

Figure 1. Biosynthesis pathways of omega-6 (n-6) and omega-3 (n-3) polyunsaturated fatty acids (adapted from de Roos et al., 2009 and Dunbar et al., 2014)

In many European countries, estimates of EPA+DHA intake are rather scarce. Mean dietary intakes of these fatty acids among adults have recently reported a daily intake of 265 mg in Austria, 380 mg in France, 250 in Germany and 90 mg in The Netherlands (EFSA, 2009). Recommendations of EPA + DHA intake from international authorities range 200–650 mg per day and are based on the convincing inverse relationship observed between its consumption and a decreased risk of CVD (WHO, 2003, EFSA, 2005). The American Heart Association (AHA) estimates based on consumption of one portion (125 g) of oily fish (2 g EPA + DHA per 100 g on average) and one portion of lean fish (0.2 g/100 g) result in an approximate intake of 3 g of DHA + EPA per week or 430 mg per day. This association also established intakes of 1 g of EPA + DHA from fish or fish oils for subjects with clinical history of CVD and a

2-4 g supplement for subjects with high blood triglycerides which produces typical 20-40 % reductions (Kris-Etherton, 2003). The French authority for food safety also established recommendations for adult men (500 mg/day) and adult women (400 mg/day) (AFFSA, 2003). Interestingly, although the above mentioned recommended daily intake (RDI) currently used in Europe are well above this value (400-450 mg/day), EFSA argues that the most recent evidence shows that, when only healthy subjects are considered, the intake of EPA+DHA is negatively related to cardiovascular (CV) risk in a dose-dependent way up to 250 mg/day that means 1–2 servings of oily fish per week (EFSA, 2009). According to Su (2009) indicates that 7% erythrocyte DHA is the appropriate target amount needed to prevent affective disorders. In order to achieve the level, the dosage for children should be 400 to 700 mg DHA per day, and for adults 700 to 1000 mg per day. These amounts are consistent with the levels of DHA consumption in the populations that consume large amounts of fish cited above. Marangell et al., (2004) reported that fish oil supplementation (a combination of EPA and DHA 2.96 g per day), starting between 34 and 36 weeks of pregnancy, did not prevent the occurrence of postpartum depression (PPD) in women who had experienced it after previous pregnancies. They observed postpartum depressive episodes in four of seven subjects. The expected rate of recurrence of postpartum depression was 20-60 % reported by Wisner et al. (2001). Epidemiological studies indicate that humans evolved on a diet with a ratio of omega-6/omega-3 polyunsaturated fatty acids of approximately 1, compared to the modern typical western diet where the ratio increased to 10-30:1 (Simopoulos, 2006). This change attributed to the increased intake of omega-6 fatty acids coupled with a decreased intake of omega-3 fatty acids, particularly EPA and DHA. Unfortunately, a high omega-6:omega-3 ratio promotes the pathogenesis of many diseases, including CVD, cancer, and inflammatory diseases, whereas increased levels of long-chain omega-3 fatty acids (lower omega-6:omega-3), with an optimal ratio of 2-4:1, exert suppressive effects due to eicosanoid function (Simpoulos, 2002). For CVD prevention, the National Heart Foundation (NHF) of Australia and the American Heart Association (AHA) ecommend two to three servings of oily fish a week or 500 mg/day of EPA/DHA for adults (Colquhoun et al., 2008). Researchers from Taiwan Medical University published a recent study in which they found that a mixture of 4.4g EPA and 2.2g DHA alleviated depression (versus placebo) in those with treatment-resistant depression. This was a two-month study involving patients who were on anti-depressants that were not working. As with the other omega-3 studies discussed, the fish oil was well-tolerated and no adverse events were reported by Su (2003).

It is well recognized that n-6 PUFAs, especially arachidonic acid are needed for fetal and infant brain development and that n-6 linoleic acid is needed to prevent essential fatty acid deficiency states in humans. Also n-6 PUFAs can contribute to decreasing some factors related to human cardiovascular disease (Deckelbaum and Calder, 2010). The n-6 PUFAs are known to have pro-inflammatory activity which could play important roles in immune function. Typically, human inflammatory cells contain high proportions of the n-6 PUFA arachidonic acid and low proportions of n-3 PUFA. The significance of this difference is that arachidonic acid is the precursor of two-series prostaglandins and four-series leukotrienes, which are highly-active mediators of inflammation (Calder, 2002). The n-3 long chain PUFA content of plasma phospholipids is significantly increased after patients were fed a low n-6 PUFA diet. These data demonstrate that reducing n-6 PUFA intake for 4 weeks increases n-3 long chain PUFA status in humans in the absence of increased n-3 PUFA intake (Wood et al., 2014) Some negative effects have been reported to be associated with adverse events excessive levels of n-6 including associations with obesity (Ailhaud et al., 2008, Anderson et al., 2010, Massiera et al., 2003, Muhlhausler and Ailhaud, 2013), diabetics, cancer, depression etc. (Turan et al., 2013) although more studies are needed to clarify the relationship with n-3 and n-6 mechanisms of these associations.

Conclusions

The continuing accumulation and publication of evidence of the beneficial health effects of PUFAs captured the attention, not only of the medical that is generally becoming aware of the importance of diet to general physical and mental wellbeing. In fact, the two PUFA families that n-3 and n-6 are biologically connected through the cascade of enzymatic transformations that starts immediately after the intake of precursors from the diet. Moreover, after gathering evidence of insufficient intake of omega-3 fatty acids from the diet, the attention to the fatty acid composition present in food increased, thus, leading to an interest in the n-6/n-3 balance as a measure of a healthy diet. Omega-3 and Omega-6 effects different issues in human health. n-6/n-3 ratio in diet is very important for health. The main dietary sources long chain n-3 PUFAs in nature are fish and marine animals and fish oils for healthy and balanced diets. At least, common views are 1–2 servings of oily fish per week.

Table 1: Summary of some studies with health benefits of n-3 (omega-3)

References	Impact On Health	Investigations
Dyerberg et al. 1975, 1978	Low incidence of cardiovascular heart disease	Eskimos consume more LC ω-3 PUFAs; lowered plasma triglyceride and cholesterol levels; lowered LDL and VLDL; high immunereactive anti-thrombin AT-III, heparin cofactor
Mozaffarian et al. 2005	Reduction of chronic heart failure and prevention of cardiovascular disease	EPA + DHA reduce risk of coronary heart disease including acute coronary related sudden death
Biondo et al. 2008	Alters toxicity of chemotherapeutic drugs	EPA and/or DHA alters toxicity and activities of chemotherapeutic drugs
Cicero et al. 2009	Reduced blood pressure	n-3 PUFAs reduce blood pressure via effect on endothelial function
Makhoul et al. 2011	Effects on obesity	Triglycerides and C-reactive protein attenuated in adults with high red blood cell EPA and DHA
Rix et al. 2013	Decrease in cardiac arrhythmia	Evidence for prevention and treatment of atrial fibrillation
Nikolakopoulou et al. 2013	Skin and oral cancer	Selectively inhibits growth and induces cell death in early and late stage cancer
Tousoulis et al. 2014	Lowered triglycerides	n-3 PUFAs lower triglyceride concentrations up to 27%
Tousoulis et al. 2014	Improved endothelial function	Reduce adipogenesis and lipogenesis in adult rodents n-3 PUFAs improve endothelial vasomotor function via improved vasodilation and improved systemicarterial compliance anti-inflammatory effect

References

Adkins, Y., Kelley, D.S. (2010): Mechanisms underlying the cardioprotective effects of omega-3 polyunsaturated fatty acids. *Journal of Nutritional Biochemistry*, 21: 781792.

Agence Français de Sécurité Sanitaire des Aliments (AFFSA) (2003): The omega-3 fatty acids and the cardiovascular system: nutritional benefits and claims;, http://www.afssa.fr/ftp/afssa/basedoc/rapportomega3.pdf.

Ailhaud, G., Guesnet, P., Cunnane, S.C. (2008). An emerging risk factor for obesity: does disequilibrium of polyunsaturated fatty acid metabolism contribute to excessive adipose tissue development? *British Journal of Nutrition*, 100:461-470.

Anderson, A.K., McDougald, D.M., Steiner-Asiedu, M. (2010). Dietary trans fatty acid intake and maternal and infant adiposity. *European Journal of Clinical Nutrition*, 64: 1308-1315.

American Heart Association (AHA) Scientific Statement (2006): Diet and lifestyle recommendations revision: a scientific statement from the American Heart Association Nutrition Committee. *Circulation*, 114: 82-96.

Arterburn LM, Hall EB, Oken H. (2006). Distribution, interconversion, and dose response of n-3 fatty acids in humans. *American Journal of Clinical Nutrition*, 83: 1467-1476.

Biondo, P.D., Brindley, D.N., Sawyer, M.B., Field, C.J. (2008): The potential for treatment with dietary long-chain polyunsaturated n-3 fatty acids during chemotherapy. *Journal of Nutritional Biochemistry*, 19: 787-796.

Calder, P.C. (2002): Dietary modification of inflammation with lipids. *Proceedings of the Nutrition Society*, 61: 345–358.

Cicero, A.F., Ertek, S., Borghi, C. (2009): Omega-3 polyunsaturated fatty acids: their potential role in blood pressure prevention and management. *Current Vascular Pharmacology*, 7: 330-337.

Colquhoun, D., Ferreira-Jardim, A., Udell, T., Eden, B. (2008): Fish, fish oils, n-3 polyunsaturated fatty acids and cardiovascular health. Review of Evidence. *National Heart Foundation of Australia*, 1-54.

Deckelbaum, R.J., Calder, P.C. (2010): Dietary n-3 and n-6 fatty acids: are there 'bad' polyunsaturated fatty acids? *Current Opinion in Clinical Nutrition and Metabolic Care*, 13: 123-124.

Densupsoontorn, N., Carpentier, Y.A., Racine, R., Murray, F.M., Seo, T., Ramakrishnan, R. (2008): CD36 and proteoglycan-mediated pathways for (n-3) fatty acid enriched triglyceride-rich particle blood clearance in mouse models in vivo and in peritoneal macrophages in vitro. *Journal of Nutrition*, 138: 257-261.

De Roos, B., Mavrommatis, Y., Brouwer, I.A. (2009): Long-chain n-3 polyunsaturated fatty acids: new insights into mechanisms relating to inflammation and coronary heart disease. *British Journal of Pharmacology*, 158: 413-428.

Dunbar, B.S., Bosire, R.V., Deckelbaum R.J. (2014): Omega 3 and omega 6 fatty acids in human and animal health: An African perspective. *Molecular and Cellular Endocrinology* 398: 69-77

Dyerberg, J., Bang, H.O., Hjorne, N. (1975): Fatty acid composition of the plasma lipids in Greenland Eskimos. *American Journal of Clinical Nutrition*, 28: 958–966.

Dyerberg, J., Bang, H.O., Stoffersen, E., Moncada, S., Vane, J.R. (1978): Eicosapentaenoic acid and prevention of thrombosis and atherosclerosis? *Lancet* 2: 117–119.

EFSA (2005): Opinion of the Scientific Panel on Dietetic Products, Nutrition and Allergies on a request from the Commission related to nutrition claims concerning omega-3 fatty acids, monounsaturated fat, polyunsaturated fat and unsaturated fat. *European Food Safety Authority Journal*, 253: 1–29. http://www.efsa.eu.int/science/nda/nda opinions/catindex en.html.

EFSA (2009): Opinion of the scientific panel on dietetic products, nutrition and allergies on a request from the Commission related to labelling reference intake values for n−3 and n−6 polyunsaturated fatty acids. *European Food Safety Authority Journal*, 1176: 1-11.

Francois, C.A., Connor, S.L., Bolewicz, L.C., Connor, W.E. (2003): Supplementing lactating women with flaxseed oil does not increase docosahexaenoic acid in their milk. *American Journal of Clinical Nutrition,* 77: 226-33.

Freeman, M.P. (2006): Omega-3 fatty acids and perinatal depression: A review of the literature and recommendations for future research Prostaglandins, *Leukotrienes and Essential Fatty Acids* 75: 291-297.

Goyens, P.L., Spilker, M.E., Zock, P.L., Katan, M.B., Mensink, R.P. (2005): Compartmental modeling to quantify alpha-linolenic acid conversion after longer term intake of multiple tracer boluses. *Journal of Lipid Research,* 46: 1474-1483.

Holub, D. J., Holub, B.J. (2004): Omega3 fatty acids from fish oils and cardiovascular disease. *Molecular and Cellular Biochemistry*, 263: 217-225.

Kris-Etherton, P.M., Harris, W.S., Appel, L.J. (2002): American Heart Association, Nutrition Committee. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. *Circulation*, 106: 2747-2757.

Kris-Etherton, P.M. (1999): Monounsaturated fatty acids and risk of cardiovascular disease. *Circulation*, 100: 1253-1258.

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: 151-152.

Makhoul, Z., Kristal, A.R., Gulati, R., Luick, B., Bersamin, A., O'Brien, D., et al. (2011): Associations of obesity with triglycerides and C-reactive protein are attenuated in adults with high red blood cell eicosapentaenoic and docosahexaenoic acids. *European Journal of Clinical Nutrition*, 65: 808-817.

Marangell, L.B., Martinez, J.M., Zboyan, H.A. Chong, H., Puryear, L.J. (2004): Omega-3 fatty acids for the prevention of postpartum depression: negative data from a preliminary, open-label pilot study, *Depress Anxiety* 19(1): 20-23.

Massiera, F., Saint-Marc, P., Seydoux, J., Murata, T., Kobayashi, T., Narumiya, S., et al. (2003): Arachidonic acid and prostacyclin signaling promote adipose tissue development: a human health concern? *Journal of Lipid Research,* 44: 271-279.

McGregor, J.A., Allen, K.G.D., Mary, A.H., Reece, M., Wheeler, M., French, J.I., Morrison, J. (2001): The omega-3 story: nutritional prevention of preterm birth and other adverse pregnancy outcomes. *Obstetrical & Gynecological Survey*, 56: 1-13.

Mozaffarian, D., Ascherio, A., Hu, F. B., Stampfer, M. J., Willett, W. C., Siscovick, D. S. (2005): Interplay between different polyunsaturated fatty acids and risk of coronary heart disease in men. *Circulation*, 111: 157–164.

Muhlhausler, B.S., Ailhaud, G.P. (2013): Omega-6 polyunsaturated fatty acids and the early origins of obesity. *Current Opinion in Endocrinology, Diabetes and Obesity,* 20: 56-61.

Murray-Taylor, F.M., Ho, Y.Y., Densupsoontorn, N., Chang, C.L., Deckelbaum, R.J., Seo, T. (2010): n-3, but not n-6 lipid particle uptake requires cell surface anchoring. *Biochemical and Biophysical Research Communications,* 392: 135-139.

Nikolakopoulou, Z., Nteliopoulos, G., Michael-Titus, A.T., Parkinson, E.K. (2013): Omega-3 polyunsaturated fatty acids selectively inhibit growth in neoplastic oral keratinocytes by differentially activating ERK1/2. *Carcinogenesis*, 34: 2716-2725.

Rubio-Rodríguez, N., Beltrán, S., Jaime, I., de Diego, M.S., Sanz, T.M., Carballido, J.R. (2010): Production of omega-3 polyunsaturated fatty acid concentrates: A review, *Innovative Food Science and Emerging Technologies* 11: 1-12.

Rix, T.A., Christensen, J.H., Schmidt, E.B. (2013): Omega-3 fatty acids and cardiac arrhythmias. *Current Opinion in Clinical Nutrition and Metabolic Care,* 16: 168-173.

Simopoulos, A.P. (2002): Omega-3 fatty acids and cardiovascular disease: The epidemiological evidence. *Environmental Health and Preventive Medicine*, 6: 203-209.

Simopoulos, A.P. (2006): Evolutionary aspects of diet, the omega-6/omega-3 ratio and genetic variation: nutritional implications for chronic diseases. *Biomedicine and Pharmacotherapy*, 60: 502-507.

Su, K.P., Shih-Yi, H., Chi-Chiang, C., Winston, W.S. (2003): Omega-3 fatty acids in major depressive disorder. A preliminary double-blind, placebo controlled trial. *European Neuropsychopharmacology*, 13(4): 267-271.

Su, KP. (2009): Biological mechanism of antidepressant effect of omega-3 fatty acids: How does fish oil act as a 'mind-body interface'?, *Neurosignals*, 17: 144-52.

Sontrop, Jessica, Campbell, M. Karen. (2006): ω-3 polyunsaturated fatty acids and depression: A review of the evidence and a methodological critique, *Preventive Medicine*, 42: 4-13.

The World Health Organisation (2003): Diet nutrition and the prevention of chronic diseases. Report of the WHO/FAO Joint Expert Consultation, WHO, Technical Report Series 916.

Tousoulis, D., Plastiras, A., Siasos, G., Oikonomou, E., Verveniotis, A., Kokkou, E. (2014): Omega-3 PUFAs improved endothelial function and arterial stiffness with a parallel antiinflammatory effect in adults with metabolic syndrome. *Atherosclerosis*, 232: 10-16.

Turan, H., Erkoyuncu, İ., Kocatepe, D. (2013): Omega-3, Omega-6 Yağ Asitleri ve Balık. *Yunus Araştırma Bülteni*, 2:41-46.

Yaqoob, P., Shaikh, S.R. (2010): The nutritional and clinical significance of lipid rafts. *Current Opinion in Clinical Nutrition and Metabolic Care*, 13: 156-166.

Vessby, B., Unsitupa, M., Hermansen, K., Riccardi, G., Rivellese, A. A., Tapsell, L. C. (2001): Substituting dietary saturated for monounsaturated fat impairs insülin sensitivity in healthy men and women: the KANWU Study. *Diabetologia*, 44:312–319.

Visentainer, J.V., Noffs, M. D'A., Carvalho, P. O., de Almeida, V.V., de Oliveira, C.C., de Souza, N.E. (2007): Lipid content and fatty acid composition of 15 marine fish species from the south coast of Brazil. *Journal of American Oil Chemist's Society*, 84: 543-547.

Wang, C., Chung, M., Lichtenstein, A. (2004): Effects of omega-3 fatty acids on cardiovascular disease. Evidence report/technology assessment no. 94 (prepared by Tufts-New England Medical Center Evidencebased Practice Center, under contract no. 290-02-0022). AHRQ Publication No. 04-E009-2. 94. Rockville, MD, Agency for Healthcare Research and Quality.

Wisner, K.L., Perel, J.M., Peindl, K.S., Hanusa, B.H., Findling, R.L., Rapport, D. (2001): Prevention of recurrent postpartum depression: a randomized clinical trial, *Journal of Clinical Psychiatry*, 62(2):82-86.

Wood, K.E., Lau, A., Mantzioris, E., Gibson, R.A., Ramsden, C.E., Muhlhausler, B.S. (2014): A low omega-6 polyunsaturated fatty acid (n-6 PUFA) diet increases omega-3 (n-3) long chain PUFA status in plasma phospholipids in humans. Prostaglandins Leukot. *Essential Fatty Acids*, 90: 133-138.