Resources and Bioactivities of Polyunsaturated Fatty Acids

Xiao-Xi Ouyang¹, Tong Zhou¹, Sha Li², Pei Zhang¹, Ren-You Gan³, Hua-Bin Li¹, *

¹ Guangdong Provincial Key Laboratory of Food, Nutrition and Health, Department of Nutrition, School of Public Health, Sun Yat-Sen University, Guangzhou 510080, China
² School of Chinese Medicine, The University of Hong Kong, Sassoon Road, Hong Kong, China
³ School of Biological Sciences, The University of Hong Kong, Pokfulam Road, Hong Kong, China

* Author to whom correspondence should be addressed; E-Mail: lihuabin@mail.sysu.edu.cn; Tel: +86-20-87332391; Fax: +86-20-87330446.

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Abstract: Polyunsaturated fatty acids are essential to human health, in particular ω-3 polyunsaturated fatty acids. However, they cannot be produced by the body, and only can be obtained from the dietary sources such as vegetable oils, fish oils, and microalgae. Polyunsaturated fatty acids possess antioxidant, anti-inflammation and antibacterial activities, and have positive health effects in the treatment of chronic diseases, such as cardiovascular disease, type 2 diabetes, some cancers, and obesity. This review summarizes current knowledge about dietary sources and bioactivities of polyunsaturated fatty acids, and special attention is paid to the bioactivities.

Keywords: polyunsaturated fatty acids; bioactivity; antioxidant; cardiovascular disease; cancer.

1. Introduction

Polyunsaturated fatty acids (PUFAs) containing two or more double bonds have been attracted the public attention for their health benefit. As the research developing, the veil of PUFAs was uncovered. PUFAs are important components of organisms for maintaining the structure and function...
of cell membrane (Calder et al., 2010). In addition, PUFAs as precursor take part in the synthesis of several biomolecules such as eicosanoids and prostaglandin (Radwan et al., 1991). They participate in a variety of physiological processes and play a key role in metabolism (Gill et al., 1997; Pereira et al., 2012).

PUFAs are a big family and contain a lot of family members. N-3 PUFAs and n-6 PUFAs are the major members. PUFAs are commonly biosynthesized via an extension of the saturated-fatty acid pathway in invertebrate (Gill et al., 1997). Meanwhile, almost all of the required long chain unsaturated fatty acids are synthesized by vertebrates through elaborating linoleic acid (LA) and α-linoleic acid (ALA). These two kinds of PUFAs cannot be produced by vertebrates and only can be taken from dietary food (Burdge et al., 2002). The research showed that the long chain polyunsaturated fatty acids (LCPUFAs) synthesized in vivo can not afford to the needed (Pereira et al., 2012). Thus, dietary food is the main source of LCPUFAs. The original known food sources of PUFAs are fish and vegetables. Considering these sources are limited, scientists found several new sources of PUFAs such as microalgae which have rich and various PUFAs (Lenihan-Geels et al., 2013).

Taking PUFAs regularly is benefit for keeping health. N-3 PUFAs and n-6 PUFAs have different function in metabolism (Miles and Calder, 2012). N-3 PUFAs are the main beneficial properties of PUFAs, in particularly docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). Clinical trials suggested that the deficiency of n-3 PUFAs is the causation of many chronic diseases like cardiovascular disease (Simopoulos et al., 2002; Vafeiadou et al., 2012). Epidemical data and animal experiments supported that the PUFAs supplementation could improve the condition of inflammatory diseases and prevent the carcinogenesis (MacLennan et al., 2013). Those characteristics of PUFAs inspired the interest of researchers. The evidence from a large of studies demonstrated that polyunsaturated fatty acids possess a variety of bioactivities, such as anti-inflammatory, antioxidant, anti-aging, and antibacterial activities as well as prevention of cardiac diseases, inhibition of tumor progression, and treatment of mental disease. The most of the molecule mechanisms of those bioactivities were recognized with the development of molecule biological technique. In this review, current knowledge about dietary sources and bioactivities of polyunsaturated fatty acids is summarized, and special attention is paid to the bioactivities.

2. Dietary Sources of Polyunsaturated Fatty Acids

2.1. Marine Fish

Marine fish is well known for containing rich PUFAs, especially, EPA and DHA. It has great advantages compared with traditional vegetable oil and was considered as the major source of PUFAs. The studies showed that the best dietary source of n-3 PUFAs is seafood, particularly oily fish such as...
sardine, salmon, tuna, mackerel and herring (McManus et al., 2011). Increased fish consumption, especially of marine origin, can lead to a raised supply of n-3 LCPUFAs (Molendi-Coste et al., 2011). Fish consumption has attracted considerable interest in the past few decades in relation to their health benefits. Whereas, the marine fish source confronts daunting challenges with the increasing of fish consumption and environment changing. Fisheries are currently producing the maximum fish stocks per annum in order to supply fish for human consumption, as well as supplying feed for industrial fish farms and fish oil supplements, resulting in a unsubstantial effect on fish levels and the possibility of extinction (Dulvy et al., 2003). As a result of the pollution of the marine environment, harmful substances were accumulated in fish (Venegas-Caleron et al., 2010). Those challenges indicate a need to develop alternative, sustainable sources of very long chain polyunsaturated fatty acids.

2.2. Vegetable

For lacking of requisite enzymes, plants high in ω-3 PUFA, such as linseed, primrose, echium and hempseed, contain only shorter-chain ω-3 PUFA and none, or low levels of EPA and DHA (Miller et al., 2008). Different from marine fish, plants are rich in LA, GLA and ALA, respectively. The some plant seeds are the main vegetable sources of PUFAs. As the over consumption of fish, the plant sources of PUFAs throw light upon the research. Although the vegetable sources have low levels of EPA and DHA, the ability to use plant oils in fish feed and human supplement production would substantially reduce the impact on fish levels, introducing a much more sustainable and economical source.

In order to make good useful of the vegetable sources, amount of researches have been involved. A number of transgenic varieties of common plants such canola, soy-bean, and safflower have been developed that produce seed oils, which are enriched with EPA or DHA (Sayanova and Napier, 2011). However, it is limited by the negative attitudes toward transgenic food in certain geographical areas. The discovery of stearidonic acid (SDA) is one of the achievements. SDA is an intermediate fatty acid in the biosynthetic pathway from α-linolenic acid to VLC ω-3 PUFAs and the conversion from SDA is more efficient than from α-linolenic acid (Walker et al., 2013). Thus, the consumption of oils rich in SDA can result in an enrichment of tissues with longer chain PUFA like EPA, DPA, or DHA. SDA mainly exist in the plant seeds, such as *Echium plantagineum* seed. However, the concentration of SDA in the traditional plant seeds sources is barely satisfactory. New plant oil extracted from the seeds of *B. arvensis* was found to be a rich source of SDA (20% SDA). SDA-containing oils and oils from genetically modified plants showed that new dietary sources of ω-3 PUFA may represent viable and effective alternatives to marine oils (Surette, 2013).

2.3. Microorganism

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Microorganisms are promising as producers of various polyunsaturated fatty acids, because they possess the array of desaturase and elongase activities required for the de novo production of the various PUFAs. These lower organisms can synthesize the entire range of PUFAs and can be grown on an industry scale. For example, terrestrial and marine phycomycete fungi, especially from the Mucorales, produce GLA, AA, EPA and DHA (Gill et al., 1997). Ogawa et al. (2012) described that an oleaginous filamentous fungus Mortierella alpina 1S-4 could produce oils containing not only common n-6 and n-3 PUFAs but also rare PUFAs. In addition, some macroalgae can be considered as a potential source for large-scale production of essential PUFAs with wide applications in the nutraceutical and pharmacological industries by analyzing 17 macroalgal species from three different phyla (Chlorophyta, Phaeophyta and Rhodophyta) and assessing their fatty acid methyl esters (FAME) profile. The results showed that Rhodophytes and Phaeophytes have higher concentrations of PUFAs, particularly from the n-3 series, thereby being a better source of these compounds (Pereira et al., 2012). Microorganisms as a new star of the alternative sources of the PUFAs have been attracting much attention.

3. Bioactivities of Polyunsaturated Fatty Acids

3.1. Anti-inflammatory Activity

Polyunsaturated fatty acids could affect various functions of inflammatory responses. Inflammation is a part of the normal host response to infection and injury. Eicosanoids, cytokines, chemokines, adhesion molecules and other inflammatory molecules are frequently produced during this process. Although inflammation is a normal response, when it occurs in an uncontrolled or inappropriate manner, excessive damage to host tissues could cause diseases. The numerous studies in humans have documented the inflammation-limiting properties of ω-3 fatty acids. De Caterina et al. (1994) demonstrated that long chain n-3 PUFAs affect the cell surface expression of adhesion molecules, which are involved in interactions between leukocytes and endothelial cells. Long chain n-3 PUFAs also affect synthesis of inflammatory cytokines, a process that is regulated in part by PGE2 and 4-series LTs. The cell culture studies demonstrate that both EPA and DHA could inhibit the production of tumor necrosis factors-α (TNF-α) and interleukin-1 β (IL-1 β) by monocytes (Babcock et al., 2002; Novak et al., 2003; Siriwardhana et al., 2012). The cellular mechanisms of the anti-inflammatory action by n-3 PUFAs were summarized by Calder (2006). The work indicated that the long chain n-3 PUFAs decreased arachidonic acid and increased long chain n-3 PUFAs in inflammatory cell membrane phospholipids to improve the inflammatory phenotype by altering membrane structure, pattern of eicosanoid and resolvin synthesis, signal transduction pathways, and inflammatory gene expression.
The recognition that the long chain n-3 PUFAs have anti-inflammatory actions has led to the ideas that an absolute or relative lack of these fatty acids might contribute causally to inflammatory conditions. It might bring about clinical benefit for patients with inflammatory diseases by supplementation of the n-3 PUFAs. Dietary ω-3 fatty acids are associated with plasma biomarker levels, reflecting lower levels of inflammation and endothelial activation in cardiovascular disease and other chronic and acute diseases, including chronic renal disease, sepsis and acute pancreatitis (Rangel-Huerta et al., 2012). There is evidence of clinical benefit from trials conducted in rheumatoid arthritis and inflammatory bowel disease (IBD) (Bassaganya-Riera and Hontecillas, 2010; Miles and Calder, 2012). The supplementation trials with long chain n-3 PUFAs have been conducted in most of the inflammatory conditions.

3.2. Antioxidants Activity

Though common knowledge on fatty acids holds it that the higher degree of unsaturation the higher susceptibility to oxidation, several lines of evidence indicate that this assumption does not always hold true. For example, Doriane et al. (2008) investigated the free radical-scavenging potential of PUFAs and the production of reactive oxygen/nitrogen (ROS/RNS) species by human aortic endothelial cells (HAECs) supplemented with different fatty acids. They reported that supplementation of HAEC with polyunsaturated fatty acids of the ω3 series resulted in lower formation of ROS, as compared with cells supplemented with saturates, monounsaturates, or polyunsaturates of the ω6 series. One explanation proposed by the authors was that the n-3 PUFAs might act as indirect anti-rather than pro-oxidant in vascular endothelial cells. There are many evidences to support the antioxidant of n-3 PUFAs (Richard et al., 2008; Tai and Ding, 2010).

The mechanisms by which ω-3 PUFAs achieve their protective effect has not been well established. A proposed mechanism was that the n-3 PUFAs could impact the enzymes of oxidative process to regulate the balance of oxidative products in vivo. Cappellari et al. (2013) investigated whether treatment with n-3 PUFA reverses endothelial dysfunction and oxidative stress in experimental menopause under the background that menopause is associated with endothelial dysfunction and oxidative stress. They demonstrated that n-3 PUFA have a therapeutic benefit on menopause-associated endothelial dysfunction by reversal of alterations in membrane lipid composition induced by ovariectomy and by reduction of vascular oxidative stress. For the protective benefit of health, the supplementation of n-3 PUFAs has been used to treatment and to prevent several oxidative injury diseases such as mild cognitive impairment MID (Lee et al., 2013).

3.3. Cardioprotective Action
Dietary supplementation of DHA and EPA influences the fatty acid composition of plasma phospholipids that, in turn, may affect cardiac cell functions in vivo. The studies of n-3 PUFA on cardiovascular health intervention confirmed that the consumption of n-3 PUFA provided benefits for primary and secondary prevention of cardiovascular disease. Evidence from cellular and molecular researches indicated that the cardioprotective mechanisms by n-3 PUFA were complicated which involved anti-inflammation, proresolving lipid mediators, modulation of cardiac ion channels, reduction of triglycerides, influence on membrane microdomains and downstream cell signaling pathways and antithrombotic and antiarrhythmic effects (Adkins an Kelley, 2010; Siddiqui et al., 2008).

The ω-3 long chain-polyunsaturated fatty acids are increasingly used in the prevention and management of several cardiovascular risk factors. Much evidence from various laboratories have similarly indicated that regular n-3 PUFAs intake affects several humoral and cellular factors involved in atherogenesis and may prevent atherosclerosis, arrhythmia, thrombosis, cardiac hypertrophy and sudden cardiac death (Siddiqui et al., 2008). Masson et al. (2008) found that n-3 polyunsaturated fatty acids could prevent metabolic and vascular disorders in fructose-fed rats. This pathological status was related to high cardiovascular risk.

Recently, the mechanism by n-3 PUFAs for protecting cardiovascular is inconclusive. However, the activity of dietary n-3 PUFAs for reducing the cardiovascular disease’s risk has been accepted. The take regular n-3 PUFAs can decrease amount of the incidence of cardiovascular disease.

3.4. Anticancer Activity

The formation of tumor is a comprehensive process of many kinds of factors. There is increasing evidence that polyunsaturated fatty acids play a role in cancer risk and progression. The work of Eynard et al. (2013) suggested that long-standing consumption or dietary supplementation of ω-3 PUFAs might improve the chances of avoiding urinary tract tumor risk development. The effects of the PUFAs on anticancer involve many intricate biological processes. Different molecular mechanisms have been proposed to explain their effects, including alterations in arachidonic acid oxidative metabolism and metabolic conversion of n-3 PUFAs to novel discovered bioactive derivatives; modification of oxidative stress; changes in cell membrane fluidity and structure and altered metabolism and function of membrane proteins (Calviello et al., 2009). As the mechanisms were discovered, the beneficial effect of n-3 polyunsaturated fatty acids as chemopreventive and chemotherapeutic agents in the treatment of cancer attracted considerable interesting. Considerable knowledge has been recently gathered on the possible beneficial effects of n-3 PUFAs administered in combination with different antineoplastic drugs and radiotherapy against melanoma, leukemia,
neuroblastoma, and colon, breast, prostate and lung cancers. The efficacy of these combinations has been demonstrated both in vitro and in vivo, and clinical trials have also been conducted.

3.5. Antibacterial Activity

Long-chain polyunsaturated fatty acids are attracting attention as potential new topical treatments for Gram-positive infections due to their antimicrobial and anti-inflammatory properties. Huang et al. (2010) reported that their study found a novel bioactivity of the three major n-3 PUFAs, EPA, DHA, and ALA, and their ester derivatives and suggested that n-3 PUFA could have a positive therapeutic effect for improving oral health via their antibacterial activities, besides their anti-inflammatory effects (Huang and Ebersole, 2010). The fatty acids have attracted attention as potential therapeutic antimicrobial agents due to their potency, broad spectrum of activity and the lack of classical resistance mechanisms against the actions of these compounds. In particular, various long-chain polyunsaturated fatty acids have shown highly potent activity against Gram-positive bacteria. In another study, antimicrobial effects of six LC-PUFAs against P. acnes and S. aureus were evaluated for their potential to treat infections caused by these pathogens. The results showed that LC-PUFAs could be applied in combination with some currently available treatments to enhance therapeutic efficacy of bacterial infections (Desbois and Lawlor, 2013).

Some PUFAs could be used to treat bacterial infection. These compounds could prevent the growth of bacteria or directly kill bacteria (Desbois, 2012). Moreover, the n-3 PUFA and their derivatives have varied patterns of action against the bacteria, not limited to differences associated with the Gram-positive or Gram-negative nature of the species. The target of the n-3 PUFA could be the cellular membrane disrupting normal cell membrane functions and leading to bacterial death. The antimicrobial fatty acids could be used in medicine, agriculture and industry. In addition, PUFAs could be an innovative approach for controlling these infections in at-risk children and contribute to caries prevention strategies (Huang and Ebersole, 2010).

4. Conclusions and Prospects

With the amount of researches on polyunsaturated fatty acids, many benefits of PUFAs are well known. The consumption of food which is rich PUFAs is increasing. Marine fish are the popular food source of PUFAs for containing rich n-3 PUFAs which possess various benefits for health. However, the source is in challenge for environment pollution and excessive consumption. There is a need to exploit new food sources. The plant and microorganism attracted a lot of interests. Some studies found that stearidonic acid in some plant seeds is an intermediate fatty acid in the biosynthetic pathway from α-linolenic acid to VLC ω-3 PUFAs and the conversion from SDA is more efficient than from α-
linolenic acid. This kind of plant seeds oil could be a promising alternative food source for n-3 PUFAs. Microorganism is also well known for containing variety of PUFAs. Microalga attracted a lot of attention for having rich PUFAs with moderate ratio. The PUFAs possess many bioactivities, such as anti-inflammatory, antioxidant, antitumor, cardioprotective and antibacterial actions. Many studies are involved in the research of the benefits mechanism by PUFAs and have made some breakthrough. Recently, PUFAs have been applied in combination with some currently available treatments to enhance therapeutic efficacy. In all, PUFAs have a bright future in controlling chronic diseases and promoting health.

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