Polyunsaturated fatty acids (PUFAs) such as n-3 and n-6 fatty acids are essential nutrients which cannot be synthesized by mammals, or only to a limited extent. Therefore, they must be ingested via dietary sources. In general, it is vital to maintain an appropriate balance of n-3 and n-6 in the diet as these fatty acids work together to promote health. The n-3 fatty acids have been recognized to exhibit not only anti-inflammatory and antioxidant activities, but also exhibit anti-cancer activity, thus contributing their beneficial cardiac effects. For human consumption, current major sources of marine n-3 omega fatty acids such as eicosapentanoic (EPA) and docosahexaenoic (DHA) include salmon, mullet and mackerel. However, at the global scale, algal-based omega-3 fatty acids for human better health have been well exploited whereas salmon based or other fish-based omega-3 consumption is avoided due religious boundaries. This review explains the updates and beneficial effects of algal based omega-3 fatty acids for human health and their better effects than other omega-3 products.

[Keywords: Marine omega-3, Algae, Health beneficial effects]

Introduction

Omega-3 fatty acids such as docosahexaenoic acid (DHA) and eicosapentanoic acid (EPA) have shown great potential in human health due to their potential efficacy to treat a variety of diseases including atherosclerosis, thrombosis, arthritis, and cancer. Although marine fish have been considered rich and conventional sources for the production of EPA and DHA, the majority of the researches has focussed that production of omega-3 fatty acids is several times higher from marine algae than conventional resources. Omega-3 fatty acids (EPA & DHA) belong to polyunsaturated fatty family with a characteristic of possessing a double bond at the last 3-4 carbon position in the hydrocarbon acyl chain counting the terminal methyl carbon as number one. However, eicosapentanoic acid, docosapentanoic acid and docosahexaenoic acid are considered long chain n-3 fatty acids.

Market growth of production of omega-3 polyunsaturated fatty acid is of considerable account due to their potential use in food fabrication and as a dietary supplement. Increasing awareness of omega-3 fatty acids will certainly provide additional health-beneficial information to urban people in the near future with profound market growth. As estimated, the omega-3 market may grow with a healthy rate of 11.4% compound annual growth rate (CAGR) from 2013 through 2020 in terms of volume, whereas it is expected to reach about US$29. 4 million by 2020 growing at a CAGR of 13% in terms of value.

Production of DHA, a long-chain omega-3 polyunsaturated fatty acid from marine algae is considered as a vegetarian source of docosahexaenoic acid. DHA plays an important in brain, eye and heart health development throughout the life-cycle. Application of DHA includes several branches, including infant formula, product for pregnant and nursing women, food and beverage products and as a dietary supplement.

Although algal seaweeds contain a low amount of lipid content, large coastal deposition has defined them as a remarkable source of functional lipid. As reported previously, fish contain lipid content approximately 20% per dry weight, which may reach up to 50%, whereas algal seaweeds contain only 1-5% per dry weight of total lipid content. Recently,
it has been reported that contents of total lipid and omega-3 fatty acids may vary depending upon the blooming season for seaweeds, reaching up to 15% per dry weight, which may contain more than 40% omega-3 PUFAs per total fatty acids. Figure 1 represents how temperature control and solar energy affect to the system of omega production in the marine sea environment.

Brown algal seaweeds contain a number of bioactive and functional compounds in them, which include omega-3 PUFAs, omega-6 (arachidonic acid, fucoxanthin, fucosterol) and some other polyphenolic compounds. The carotenoids which are found in brown seaweeds show several physiological effects due to their unique molecular mechanisms.

Marine omega-3 fatty acids have a prolonged history to be used as a functional food and nutritional dietary supplement in Japan due to their potential efficacy in lowering the risk of cardiovascular incidences. These omega-3 PUFAs have been found to change multiple cardiovascular risk factors, thereby reducing atherosclerotic processes, thus confirming the protective effects on cardiovascular morbidity and mortality. The aim of this review article is to update the use and variety of algal omega-3 sources for human welfare and their health protective efficiencies.

Sources of marine omega 3 fatty acids

Omega-3 fatty acids have been found to present in a variety of fish including salmon, tuna, and halibut, as well as algal seafood, plants, and nut oils. DHA serves as a primary compound of the human brain and retina. Cold-water marine fish contain larger proportions of DHA oil. Most of the DHA in fish and complex organisms originate in photosynthetic and heterotrophic microalgae, and becomes increasingly concentrated in organisms, as they move up the food chain. Nowadays, microalgae have become significant commercial sources for the production of DHA.

On the other hand, omega oils derived from fish may contain severe chemical contaminants such as mercury, which may cause adversary effects to human health up on consumption. In addition, pungent smell of fish-derived oils makes them unattractive and unsuitable to vegetarian people due religious circumstances. In addition to microalgae, there are a variety of alternative sources available for EPA and DHA production, which include bacteria, fungi, and plants which are being explored for the commercial production. As a major hurdle, fungi need an organic carbon source and typically a prolonged growth period, whereas plants require an arable land, with a longer growth time, which have not enough enzymatic activity for the production of long-chain omega-3 fatty acids including EPA and DHA, unless genetically modified.

Microalgae are considered significant initial producers of EPA and DHA in the marine food chain with an ability of relatively faster growth under a variety of autotrophic, mixotrophic and heterotrophic conditions, and have shown great ability on the production of long-chain omega-3 fatty acid. Autotrophic and mixotrophic microalgae have great potential on the fixation of atmospheric carbon dioxide during photosynthesis, thus can easily grow on non-arable land within a short harvesting time. A comparison shows that microalgae can reach much higher EPA and DHA contents and productivities compared with other possible sources (Table 1). In particular, heterotrophic microalgae are well established as an alternative source of DHA and are added to infant milk formula or other foods. Other microalgae are used as food additives, animal feed (including aquaculture), vitamins, pigments, pharmaceutical compounds, cosmetics and potentially as a biofuel source. The development of an efficient large-scale cultivation system for the commercial production of EPA and DHA would address a major global need. Here, we review the potential of autotrophic eukaryotic microalgae as biofactories for large-scale production of omega-3 fatty acids.
Table 1-Important algae producing omega fatty acids

<table>
<thead>
<tr>
<th>Omega products</th>
<th>Algal species</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPA</td>
<td>Phaeodactylum tricornatum</td>
</tr>
<tr>
<td></td>
<td>Spirulina</td>
</tr>
<tr>
<td></td>
<td>Chlorella</td>
</tr>
<tr>
<td></td>
<td>Nannochloropsis</td>
</tr>
<tr>
<td></td>
<td>Monodus subterraneus</td>
</tr>
<tr>
<td></td>
<td>Isochrysis galbana; 24 mg EPA/L per day</td>
</tr>
<tr>
<td></td>
<td>Porphyridium cruentum; 4 mg/L per day</td>
</tr>
<tr>
<td>DHA</td>
<td>Cryptothecium cohnii</td>
</tr>
<tr>
<td></td>
<td>Schizochytrium sp.</td>
</tr>
<tr>
<td></td>
<td>Thraustochytrium aggregatum</td>
</tr>
<tr>
<td></td>
<td>Ulkenia sp.</td>
</tr>
</tbody>
</table>

Health-beneficial effects and pharmacological applications of marine omega-3

Marine oils or omega-3 oils are considered most important health supplements all over the world, including the USA, and due to this, they are used by more than a third of American adults. Marine oils derived from fish, krill, shellfish, calamari, or algae show great variations in their nutritional efficiency from those derived from plant origin, such as flaxseeds-based oils, as they possess important long chain PUFAs including EPA and DHA. Marine oils have been found to show potential efficacy for the treatment of cardiovascular and inflammatory diseases, as well as have significant effects in neurodevelopment, cognitive decline prevention, and metabolic activity improvement. However, it is to be considered that marine oils exhibit high oxidation reaction similar to other important pharmaceuticals and neutraceuticals.

Use in cardiovascular diseases:
A number of reports have shown efficacy of omega-3 fatty acids such as EPA and DHA in the creation of various cardiovascular diseases, and they are recommended on a regular basis to the patients suffering from cardiovascular diseases following myocardial infarction. However, questions have been raised about their usefulness alongside optimum medical therapies with agents proven to reduce risk of cardiac events in high-risk patients. In addition, there are some evidences for a possible pro-arrhythmic effect in subsets of cardiac patients. Moreover, there is an urgent need to optimize the dose of these PUFAs when compared with conventional supplements in order to confirm improved efficacy of these oils in the treatment of severe cardiac disorders.

Use in cancer diseases:
Nowadays, there is an increasing medical interest in using omega-3 fatty acids for the treatment of a variety of cancers and other chronic debilitating conditions, including cardiovascular disease and cognitive impairment. PUFAs have shown great potential in cancer remedies as confirmed by numerous reports. For example, low omega-3 and omega-6 fatty acid intake ratio was able to reduce risk of breast cancer and heart diseases in the western world. In Japan, Alaska and Greenland, reports confirmed that high intake of omega-3 fatty acids reduced cases of breast cancer and heart diseases. A dramatic increase in the incidence of breast cancer and cardiovascular disease in cohorts from low-incidence populations was observed who migrated to western countries and/or adopt a western diet, and demonstrated the importance of adequate DHA intake in retinal and brain development and cognitive function.

Use in inflammatory diseases:
Although some of the PFUs such as EPA, docosapentaenoic acid (DPA) and DHA can be synthesized from simpler plant-derived omega-3 fatty acids, they do not appear to be very efficient in many humans. Also, it is difficult to consider the role of marine omega-3 fatty acids within inflammatory processes without considering the roles of saturated and n-6 fatty acids. Saturated fatty acids are fatty acids without double bonds in their hydrocarbon chain, while omega-6 fatty acids belong to polyunsaturated fatty acid groups and characterized by having the last double bond between carbon numbers 6 and 7 in the hydrocarbon chain counting the terminal methyl carbon as number one. Arachidonic acid is considered as a major omega-6 fatty acid within inflammation process, which is synthesized from simpler plant-derived omega-6 fatty acids in a pathway that competes with the synthesis of EPA.

Fish and other seafoods contain a significant amount of PUFAs such as EPA, DPA and DHA, which may be collectively referred to as marine omega-3 fatty acids, where the flesh of both lean and oily fish is considered as the major reservoir of these oils. Generally, due to less consumption of fish intake by the human population, intake of n-3 fatty acids refers to a low amount of typically 0.2 g/day, and probably much lower than this. A single lean fish meal (cod fish) could provide about 0.2 to 0.3 g of marine n-3 fatty acids, while a single oily fish meal (salmon or mackerel) could provide 1.5 to 3.0 g of these fatty acids. To obtain these marine oils, flesh of oily fish (tuna) and liver of lean fish (cod) contribute...
significantly. Together, EPA and DHA as a fish oil supplement represents about 30% of total fatty acids, however, more concentrated oils are also available commercially. In fish and in traditional fish oil supplements, most of the fatty acids are present as components of triacylglycerols. Marine n–3 fatty acids are also available in other forms, such as, in krill oil, which provides EPA and DHA partly in the form of phospholipids, and as ethyl esters in pharmaceutical grade, highly concentrated preparations.\(^{31}\)

**Marine oil supplementation to improve pregnancy outcomes**

The prenatal period is critical to increase the risk of omega-3 deficiency as maternal tissue stores tend to decline\(^ {34}\), which play a significant role in the development of the fetus\(^ {35}\). Intake of marine oils as a nutritional supplement is often recommended to pregnant women to fulfil their omega-3 needs. The use of marine oil supplements during pregnancy has been studied as a possible strategy to prevent pre-term birth and helps to prevent eclampsia, as well as increases birth weight along with other potential benefits such as improving fetal brain development, and reducing the risk of cerebral palsy and postpartum depression\(^ {36,37}\). The birth outcomes concept is based on the observations of high birth weight and long gestation in communities with high fish consumption\(^ {38,39}\).

Mechanistic studies on marine oils have been investigated by several researchers which confirmed their potential health benefits for mothers and children\(^ {40}\). Based on the findings of the extensive literature survey, it can be suggested that although there is not yet enough evidence to support the routine supplementation with marine oil during pregnancy to reduce the risk of eclampsia, pre-term birth or low birth weight, pregnant women could benefit from marine oil supplementation as a means to increase the length of gestation\(^ {41}\).

**Major algae strains used for omega-3 production**

Microalgae have great ability in producing high amounts of omega-3 fatty acids. Major algal species as a rich sources of omega-3 fatty acid production specifically for the production of DHA include of *Cryptothecodinium*, *Thraustochytrium*, *Ulkenia* and *Schizochytrium*. On the other side, *Phaeodactylum*, *Chlorella*, *Monodus*, and *Nannochloropsis* algal species are considered rich sources for the production of EPA. Currently, a heterotrophic algal species *Cryptothecodinium cone* has gained a huge attention due to its enormous ability to produce the DHA, a natural health supplement of infant formula. Scientific evidences have confirmed that *Thraustochytrium aureum* possessing high amounts of fatty acid representing approximately 50% DHA of total fatty acid contents. In addition, when growing at optimal growth, algal species *Phaeodactylum tricornutum* produces high amounts of EPA comprising 30-40% of its total fatty acids. Although photoautotrophic algal species of genus *Monodus* have great ability to produce high levels of EPA, light-dependency, which results in low cell densities making them unfavorable algal species for the industrial production of EPA\(^ {42}\). Few important algal species producing omega-3 are summarized in Table 1.

**Conclusion and further prospects**

Based on recent surveys, it has been confirmed that marine omega-3 fatty acids have a number of health beneficial effects on humans as well as on marine fishes. Generally, significantly lower level of DHA exists in vegetarians and vegans compared with their omnivorous counterparts, hence, exploitation on the use of algal species as a supplement of omega-3 marine oils may open new alternative ways as natural health supplements. This study adds to the positive growing body of evidence that algal-oil is in fact a viable source of DHA, in addition to being a comparable alternative with fish-oil. This is particularly important for vegetarians, vegans and non-fish eaters in terms of obtaining optimal omega-3 fatty acid health. However, there is still need to explore the possibilities to find out new algal species as a significant producer of omega-3 fatty acids as new natural health supplements.

**References**


