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*Case Study*

# A PROMISING ALTERNATIVE TO FISH OIL SOURCE OF OMEGA 3 PRODUCTION: ROLE OF ALGAE

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**ABSTRACT**
Omega-3 fatty acids (ALA, EPA, and DHA) are important nutrients. There is a wealth of data in the medical literature about the cardiovascular benefits of omega-3 supplements. Omega-3 supplements have been shown to reduce the risk of sudden cardiac death and heart attack, slow growth of plaque in the arteries by decreasing inflammation, improve lipid levels, enhance blood pressure regulation, and reduce pulse pressure, and this has led to an increased consumption as dietary supplements. The omega-3 fatty acids are found in animals, transgenic plants, fungi and many microorganisms but are typically extracted from fatty fish, putting additional pressures on global fish stocks, some of which are dwindling. Recent interest is however on the photoautotrophic microalgae as a direct source of these omega acids as an alternative to fish oil.

**KEY WORDS:** Omega-3, algae, PUFAs, EPA, DHA.

## INTRODUCTION

Global fish stocks are declining and cannot provide a sustainable source of omega-3 fatty acids (Miller *et al*., 2008; Dulvy *et al*., 2003). An alternate source of this valuable product thus is a necessity to bridge the gap between production and demand. Worldwide, consumption of omega-3 PUFAs, estimated at 123.8 thousand metric tons worth US$2.3 billion in 2013, was forecast to be 134.7 thousand metric tons valued at US$2.5 billion in 2014. By 2020, it is projected that demand for omega-3 PUFAs globally, will reach 241 thousand metric tons with a value of US$4.96 billion, thereby posting a volume CAGR of almost 10% and a value CAGR of 11.6% between 2013 and 2020. Omega-3 (ω-3) fatty acids are polyunsaturated fatty acids (PUFAs) and essential components for the growth of humans, plants and animals (Ward and Singh, 2005). Currently, the principal source of EPA and DHA for human consumption is marine fatty fish such as salmon, mullet and mackerel (Gunstone, 1996; Whitehead, 1985). Off late, overfished stocks have increased significantly. Coupled to that presence of chemical contaminants in the water (*e.g*. mercury and other heavy metals) can be harmful to consumers (AGDAFF, 2007; Worm, *et al*., 2006; Mahaffey, 2008; Bourdon, 2010). Fish oil is also not very suitable to vegetarians due to the fishy odor. There are a variety of alternatives as EPA and DHA sources such as bacteria, fungi, plants and microalgae that are currently being explored for commercial production. Fungi require an organic carbon source and typically long growth periods (Barclay, 1994), Plants need arable land, have longer growth times and have no enzymatic activity for producing long chain PUFAs, EPA and DHA, unless genetically modified (Ursin, 2003). Algae are a diverse group of aquatic, photosynthetic organisms, generally categorized as either macroalgae (*i.e.* seaweed) or microalgae, which are typically unicellular. Among the eukaryotic, green microalgae of the class Chlorophyceae, those most widely utilized for current commercial applications belong to the genera *Chlamydomonas, Chlorella, Haematococcus, Dunaliella,* and *Nanochloropsis*. The study of these freshwater and marine algae has generated a wealth of information concerning their physiology, biochemistry, and cultivation (van den Hoek, 1995; Anderson, 2005; Harris, 2001). Successful commercial utilization of microalgae has been established in low-volume, high-value derivatives such as nutritional supplements, antioxidants, cosmetics, natural dyes, and polyunsaturated fatty acids (PUFA) (Spolaore, 2006) therefore appear to be the best choice as an alternate to fish oil. The worldwide annual production of algal biomass is estimated to be 5 million kilograms per year with a market value of about 330 USD per kilogram (Pulz and Gross, 2004).

Microalgae are the initial EPA and DHA producers in the marine food chain and can naturally grow fast under a variety of autotrophic, mixotrophic and heterotrophic culture conditions with high long chain ω-3 fatty acid production potential (Li *et al*., 2009). Autotrophic and mixotrophic microalgae fix atmospheric carbon dioxide during photosynthesis, can potentially grow on non-arable land and have short harvesting times (Li *et al*., 2009; Rubio-Rodríguez *et al*., 2010; Schenk *et al*., 2008; Chen and Chen 2006; Benemann and Oswald, 1996; Miro´n *et al*., 1999; Muller-Feuga, 2004; Ugwu *et al*., 2008).

### The need to look for alternative sources of Omega-3

Environmental scientists and researchers now predict that if urgent steps are not taken immediately to halt the depletion of our seas and oceans it will now be only a few years before there are no fish left in the ocean. This doesn't just have aesthetic and ethical implications, the fact that we've robbed our children of a rich biological heritage. The oceans, covering two thirds of the planet play an even more important role in cleaning our atmosphere than that of our dwindling rainforests. The algae and plankton that live on the surface of the sea are the true lungs of our planet and we are killing them. New toxic strains of algae are growing out of control as they uses up organophosphates and nitrogen washed into the sea. Meanwhile the beneficial algae and plankton are following the fate of the coral reefs, dying from over acidification of our sea. Fish play a vital role in balancing alkaline pH levels as they help neutralize the acid. No fish = more acid= less plankton = more $CO_2$ = less oxygen and a grave danger to life on planet Earth.

Not only do we waste fish for human consumption through catching, we devastate fish stocks by catching them to feed chickens, pigs, cows, and even other fish. We also scoop up millions of tons of fish each year to squeeze out the oil to be used by cosmetic, industrial and pharmaceutical industries. As fish become more scarce and smaller fishing fleets and trawlers have to travel further away to find less fish. As fish become more toxic, expensive decontamination and purification methods need to be deployed in an attempt to try to keep fish oil below the government's maximum levels of permitted toxins. Whole Foods pulled krill oil products off its shelves recently, citing declines of certain populations of animals relying on krill to survive. Krill are tiny relatives of shrimp, about half an inch long. A rich source of omega-3 fatty acids, they also occupy a key position near the bottom of the highly fragile oceanic food chain and represent the largest animal biomass on the planet. This made them seem a likely sustainable source for the much-coveted ingredient and a buffer against the huge ecological disasters wrought by overfishing. But the decline of animal populations that rely on krill apparently told a different story. In response to concerns over management of this natural resource, the Commission for the Conservation of Antarctic Living Marine Resources, a multinational treaty organization managing krill fisheries, issued a report changing quotas and restricting fishing areas. So if krill are off limits, and fish oil is in danger of being seen as a finite resource, how can processors expect to meet the ever-burgeoning demand for omega-3s? Here's where the good news comes in. A rush to develop more sustainable sources of EPA and DHA drew attention to algae, which naturally contain EPA and DHA. In fact, the omega-3s from krill and fish originate from the algae consumed by them or the creatures they feed on. Not only sustainable, algae can be farmed, and this form allows for such desirable labels as "vegetarian," "kosher" and even "organic."

**Microalgae are the initial Omega-3 producers**

Microalgae are by far the most abundant primary producers that can be found in most aquatic systems providing the foundation of the aquatic food chain, photosynthetically converting light energy and carbon dioxide ($CO_2$) into biomass such as carbohydrates (Park *et al*., 2011), proteins (Becker, 2007) and lipids (Harwood and Guschina, 2009). Under high nutrient supply (eutrophic conditions), algae blooms commonly occur as microalgal cell density drastically increases (Sellner *et al*., 2003). During microalgal blooms the limitation of nutrients or light halters the increase of biomass. If nutrients, but not light, are limiting, this leads to the accumulation of photosynthetic bio-products such as lipids and carbohydrates. These serve as storage products in order to survive the stressful growth limiting conditions, after which a large number of cells die (Sellner *et al*., 2003; Anderson *et al*., 2002). Algal biomass is subsequently degraded by microorganisms, consuming large amounts of oxygen. As a result an anaerobic zone in the water is formed. In extreme cases, this can lead to anaerobiosis of the entire water body, causing the death of plants and animals in the waterway; interestingly this process is also believed to have been the key factor for large-scale oceanic anoxic events that led to fossil mineral oil deposition (Schenk *et al*., 2008). Importantly, microalgae are also the primary producers of EPA and DHA that are eventually accumulated through the various trophic levels. Changes in microalgal lipid content are carried on up the food chain, impacting the growth and dietary make-up of zooplankton, crustacean larvae, mollusk and some fish (Brown, 2002). This subsequently affects the accumulation of EPA and DHA fatty acids in higher organisms and humans. Consequently, lipid profiles in microalgae play a vital role in maintaining the integrity of the world's aquatic food webs.

**Popular Omega 3 acids**

DHA (docosahexaenoic acid) is the primary compound of the human brain and retina. DHA omega-3 is to our brains as calcium is to our bones. It accounts for 97 percent of the omega-3 fats in the brain. Cold-water oceanic fish oils are rich in DHA. Most of the DHA in fish and complex organisms originates in photosynthetic and heterotrophic microalgae, and becomes increasingly concentrated in organisms, as they move up the food chain. As of today DHA is commercially produced from microalgae. DHA, produced from algae, is a vegetarian source of docosahexaenoic acid. DHA is a long-chain polyunsaturated omega-3 fatty acid and is important for brain, eye and heart health throughout the lifecycle. DHA has several applications including infant formulas, products for pregnant and nursing women, food and beverage products and dietary supplements. Because algal DHA does not come from fish, there is no risk of ocean-borne contaminants. Algal DHA provides brain, eye and heart health benefits. Omega-3 fatty acids are "good fats," and are among the most important nutrients lacking in diets today. Because our bodies don't efficiently make DHA, we need to eat foods rich in this important nutrient in order to keep our brains functioning optimally.

EPA is obtained in the human diet by eating oily fish or fish oil—*e.g.*, cod liver, herring, mackerel, salmon, menhaden and sardine. It is also found in human breast milk. Fish do not naturally produce EPA, but obtain it from the algae they consume. It is available to humans from some non-animal sources. Microalgae are being developed as a commercial source of EPA. EPA is not usually found in higher plants. Microalgae, and supplements derived from it, are excellent alternative sources of EPA and other fatty acids, since fish often contain toxins due to pollution. EPA is a polyunsaturated fatty acid (PUFA) that acts as a precursor for prostaglandin-3 (which inhibits platelet aggregation), thromboxane-3, and leukotriene-5 groups (Lewis *et al*., 2006; Naugler, and Karin 2008).

**Algal strains rich in Omega-3 fatty acids and general applications**

Microalgae can supply omega-3 fatty acids at high concentrations. Species of *Crypthecodinium*, *Thraustochytrium*, *Ulkenia* and *Schizochytrium* are rich the omega-3 fatty acid DHA, while species *of Phaeodactylum*, *Chlorella*, *Monodus*, and *Nannochloropsis* are rich in EPA. *Crypthecodinium cohnii* is a heterotrophic algal species that is currently used to produce the DHA used in many infant formulas. Research efforts have revealed that approximately 50% *Thraustochytrium aureum*'s total fatty acids are DHA. *Phaeodactylum tricornutum* is a high EPA-producing algal species with EPA comprising 30-40% of its total fatty acids when grown using optimum culture conditions. *Monodus* species are photoautotrophic algae that can produce high levels of EPA, but the dependence on light results in low cell densities making them unfavorable species to use in the industrial production of EPA. The microalga *Pavlova lutheri* is a potential source of economically valuable docosahexaenoic and eicosapentaenoic acids. There is an extensive number of algal species and each shows variability in the synthesis of EPA and DHA (Doughman *et al*., 2007; Kyle, 2001). *Schizochytrium* sp., a heterotrophic thraustochytrid, produces elevated quantities of DHA and minimal levels of EPA (Doughman *et al*., 2007). *Schizochytrium* sp. is currently used in commercial products including infant formulas, food additives, cosmetic and pharmaceutical products (Sijtsma and de Swaaf, 2004). One study investigating the thraustochytrid *Thraustochytrium* sp. demonstrated high DHA synthesis of up to 35% total fatty acids. Other beneficial aspects of this strain include tolerance to high sodium chloride concentrations and production of several carotenoids (Sijtsma and de Swaaf, 2004). Additional studies have analyzed *Cryptocodinium cohnii*, another high-DHA synthesizing microalgae, and such oils are also used in commercial products (Kyle, 2001). Conversely to *Schizochytrium* sp., *Cryptocodinium* sp. and other autotrophs and mixotrophs can fix carbon dioxide, indicating cost-efficiency and sustainability.

**Health benefits of Algae produced Omega-3 fatty acids**

Thousands of studies over several decades give strong evidence that omega-3s can help keep the cardiovascular system healthy while protecting against cancer and birth defects and countering symptoms of diabetes, arthritis, cognitive decline, depression and a number of other diseases. Omega-3 fatty acids, such as DHA, have been shown to promote good health. Research suggests that DHA may support a healthy pregnancy; support length of gestation; support visual development and function; support cognitive development and function; support cardiovascular health; reduce risk of dementia; reduce risk of Alzheimer's disease, improve memory. Omega-3 fatty acids represent an important structural component of human cell membranes, particularly neuronal cells. The consumption of EPA and DHA supplements has been shown to prevent cardiovascular, nervous system and inflammatory conditions. Regular consumption of ω-3 fatty acids can help reduce the risk of hypertension, thrombosis, myocardial infarction and cardiac arrhythmias. This occurs because ω-3 fatty acids increase the high-density lipoprotein/ low-density lipoprotein (HDL/LDL) ratio and decrease the total cholesterol/HDL ratio( Stulc and Ceska, 2001). Omega-3 fatty acids have also demonstrated positive effects on brain function and the nervous system. In pregnant women, the adequate intake of EPA and DHA is crucial for healthy development of the fetal brain (Bourre, 2007). In infants, arachidonic acid (ARA), an omega-6 fatty acid and DHA are also required for normal growth and functional development. Interestingly, increased consumption of DHA may also diminish the severity of depression and schizophrenia (Jiang *et al*., 2012). Immuno modulatory effects have been observed when ω-3 fatty acids were used in the treatment of inflammatory conditions such as rheumatoid arthritis, Crohn's disease, ulcerative colitis, psoriasis, asthma, lupus and cystic fibrosis (Simopoulos, 2002; Naugler and Karin 2008). Children ingesting Omega 3 more than once a week had a lower probability of suffering from asthma. Increasing the levels of DHA and EPA in patients with rheumatoid arthritis and ulcerative colitis has also been found to reduce pain and improve conditions. There is currently therefore a large demand for microalgae in the nutraceutical and pharmaceutical industry due to their health-promoting effects. Microalgal-derived PUFA, such as ARA and DHA are added as fortifications to infant formulae-an industry that is worth $10 billion per annum alone. To date, microalgal extracts can be found in many face and skin care products, e.g. anti-aging cream, refreshing or regenerative care products, sun cream, emollient and anti-irritant in peelers. Dermochlorella is actually extracted from *Chlorella vulgaris*, which can stimulate collagen synthesis in skin supporting tissue regeneration and wrinkle reduction. Protulines is a protein-rich extract from *Arthrospira* (*Spirulina*), which helps combat early skin aging, exerting a tightening effect and preventing wrinkle formation.

**Algae omega-3 Vs fish omega-3 –The benefits of DHA-rich algal oil**

Is algae DHA as effective at conveying the heart-healthy properties as the DHA we derive from fish oil? Many studies suggest the answer is yes, but a comprehensive review of the literature was needed. The research teams examined the relation between algal DHA supplementation and cardiovascular disease risk factors, triglycerides, LDL cholesterol and HDL cholesterol. They found that supplementation with algal DHA reduced triglycerides and raised HDL-cholesterol. This was similar to what had been reported. However, algal DHA also raised concentrations of LDL-cholesterol, although the increase was accompanied by a change in the type of LDL cholesterol to the larger, less-atherogenic form. Further research is recommended because many of the studies reviewed were funded by industries. For now, DHA from algae seems to be a sustainable, alternative source of DHA that can satisfy both the demands of consumers and the needs of vegetarians, as well as fulfilling most, if not all, the health benefits currently established with omega 3s.

**Market Size and Market Value**

The market revenue of omega-3 fatty acids was US$ 1.5 billion in 2010. This is expected to grow at a compounded annual growth rate (CAGR) of 13.8 percent between 2011 and 2016. The market for omega-3 ingredients have been growing between 10 and 18 percent across different regions in the globe, and marine source omega-3 ingredients contribute to 90% of the estimated revenues of US $2 billion globally in 2013. Replacing fish oil (approx. 1 million tons a year) by algal products completely would require an annual production of 2.5-3.5 million tons of algae. The current wholesale market price for algae omega-3 oil is about US$ 140/kg which is higher than the pricing for fish oil derived products. The Global Organization for EPA and DHA estimated that the global market for EPA and DHA omega-3 oils exceeded 85,000 t in 2009 and was estimated to grow to 135,000-190,000 t by 2015. Present worldwide annual demand for eicosapentaenoic acid (EPA) is claimed to be about 300 metric tons production from *Phaeodactylum cornutum*, which contains about 2% eicosapentaenoic acid would require production from 15,000t of algal biomass. The DSM owned company Martek producing omega- 3 fatty acid DHA had a net sale of US $450 million in 2010 and just $17.05 million were sales to food and beverage customers. The main part was sold to the infant formula makers and dietary supplements trade. Market Distribution by Region- Europe is expected to show a greater acceptance of algal oils in the near future and grows faster than North America, where algal oils are well established.

**Some key factors to look out for when choosing an Omega-3 product: Toxins, Toxicity, Poisons, and Contamination**

A few years ago a number of retailers including Boots the chemist had to withdraw cod liver oil, fish oil products because they had levels of toxins ubiquitously found in the sea that were above the safety levels set by the UK Government. Humans treat the oceans like a giant sewer, a giant global cesspit for all humanity. The trouble is with contamination, like BSE, if you don't look for it you won't find it and it's quite unusual for products like this to be officially tested. The other problem is that even though low levels of toxins in fish oil may pass the regulatory limits, and not be dangerous on their own; no-one seems to have considered what cumulative amounts of different toxins, added together in a cocktail of poisons, can have on the body. What effects do combinations of these different toxins have on our risk of cancer for instance?

Some known toxins are not even officially tested for despite prolific traces found in fish through independent testing. The best strategy to avoid risk is to avoid all fish oil products and only choose products that have pure EPA and DHA in them that have been purified. Cod liver oil in particular is from the liver of the fish and is the oil filter that protects the fish, so why would you consume the part of the fish that is likely to have the most amounts of toxins. Algal oil is farmed in a controlled environment that avoids contamination from the sea and is then filtered to separate the key EPA and DHA parts of the Omega-3 oil that are so beneficial for optimal health.

**CONCLUSION**

Over the past decade, algae biotechnology has grown steadily into a global industry with increasing numbers of entrepreneurs attempting to utilize its biochemical diversity for a wide array of applications. There are approximately 40,000 algal species, only a few thousand strains are kept in collections, a few hundred are investigated for chemical content and approximately half a dozen are cultivated in industrial quantities. Therefore, continued isolation and screening of microalgae is required, as well as more in depth studies into algal physiology, biochemistry and genetics. Meanwhile the processes for algae cultivation, harvesting and oil extraction need to be further improved in efficiency and costs. As omega-3 fatty acids are one of the most valuable products from microalgae, they are likely to be the "game-changer" towards large-scale economical microalgae cultivation that will catalyze the production of other important algal bio-products. A newly released 410-page global market report reviews, analyzes and projects the potential for marine algal omega-3 polyunsaturated fatty acid ingredients for global and regional markets including North America, Europe, Asia-Pacific and Rest of World. The regional markets further analyzed for 13 independent countries across North America: The United States and Canada; Europe: Germany, France, Italy, Spain, Norway, Denmark, The United Kingdom and rest of Europe; Asia-Pacific: China, Japan, South Korea, India and Rest of Asia-Pacific. Algae-derived oils are vegetarian-friendly and easy to grow on a large scale due to their small size. Superfluous lipid and protein during algal growth may be used as biodiesel and biomass for oil sources and animal feed, respectively (Adarme-Vega *et al*., 2012; Subhadra, and Grinson, 2011). This highlights the sustainable benefits of algae and the many potential gains from creating algal bio-factories.

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