



Advances in sources, production and delivery technologies enhancing Omega-3 Fatty Acids applications in food industry



I. Introduction

Omega-3 fatty acids (FAs) are emerging as some of the most widely used beneficial compounds in human health. The three long-chain polyunsaturated Omega-3 FAs commonly recognized as having health benefits are Docosahexaenoic acid (DHA, 22:6, n-3), Eicosapentaenoic acid (EPA, 20:5, n-3) and Alpha linolenic acid (ALA, 18:3, n-3). They are classified as essential fatty acids because the body cannot synthesize them and must be obtained from the diet but they are necessary for the regular metabolic activities.

DHA is an important component of neural membranes, comprising 40 percent of the polyunsaturated fatty acids (PUFAs) in the brain and 60 percent in the retina. DHA is important for fetal brain development, optimal development of motor skills and visual activity in infants, lipid metabolism in children and adults, and cognitive support in the elderly¹. EPA and DHA have shown to lower blood triglycerides and also exert beneficial effects in inflammatory conditions². ALA is part of the metabolic pathway that leads to other Omega-3 fatty acids, but the conversion rate in the body is very low.

II. Market for DHA/ Omega-3 Fatty Acids:

Omega-3 FAs are promising functional ingredients in the food and beverage industry. Various scientific studies supporting multiple health benefits, increased awareness among the consumers and advances in technological capabilities to incorporate Omega-3 oils into wide category of food products and beverages have contributed to the market growth for DHA/ Omega-3 FAs. The improved stability, application development, formulations to suit wider product range and advancements in delivery methods in different types of products, other than capsules/soft gels as supplements, are major drivers for the growth of Omega-3 FAs in food industry. There is also a surge in activities by industry seeking alternate sources, developing production systems and processing of Omega-3 FAs. New product development in the Omega-3 FAs space is driven not only by new finished products, but also new sources as well. Plant sources like Flax, Chia are playing a major role in the new product roll outs by the food industry.

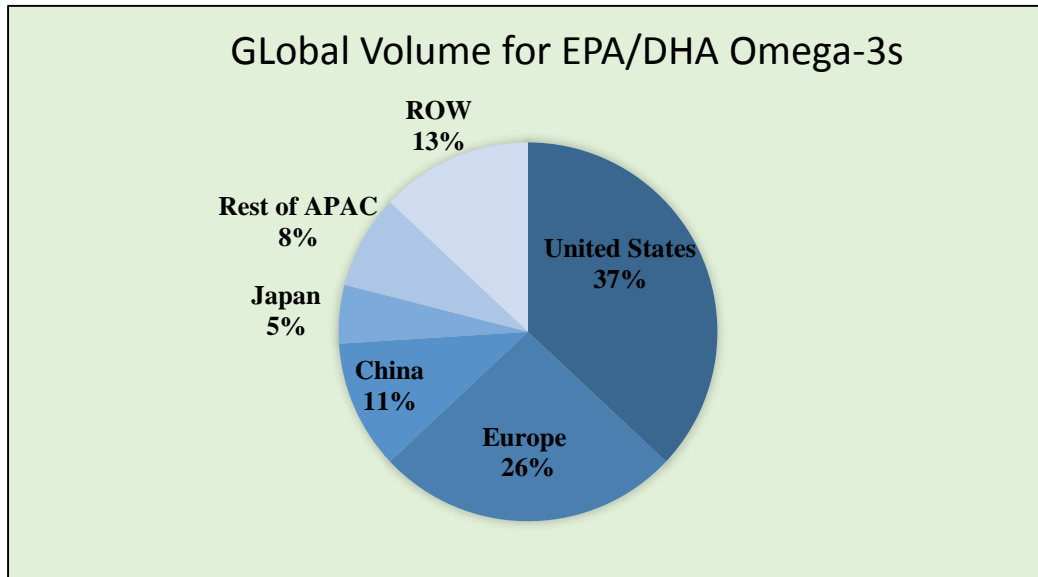
The volume of EPA and DHA oils consumed globally in 2013 was 89,000 metric tons of oil corresponding to a value of \$1.72 billion and USA was leading with 37% of volume consumption (as per Global Organization for EPA and DHA Omega-3s (GOED), 2014). However, the global sales of Omega-3 FAs finished products is expected to reach US\$34.5 billion by 2016³. According to Euromonitor International, global retail value sales of fortified/functional foods and beverages featuring Omega-3 FAs as the "key functional ingredient", stood at US\$2.4 billion in 2014,

¹ Monograph 2009, Alternative Medicine Review 14: 391-399

² Kagan et al., 2013. Lipids Health Dis. 12: 102

³ SupplySide Omega -3 Insights, March 2014

compared to US\$3.6 billion for fish oils/Omega-3 FAs dietary supplements. Dairy and spreadable oils and fats were the most popular categories for sales in 2014.



Source: GOED, 2014.

BASF, Croda, Cargill, DSM, Lonza, Epax are some of the leading suppliers of Omega-3 FAs and few companies like DSM have both fish and algal source Omega-3 FAs in their product portfolio catering to different market segments. The earliest applications of Omega-3 FAs in food were limited to spreads and yoghurts because of flavor and stability considerations. With advances in delivery technologies, improved flavor and taste, Omega-3 FAs from all the available sources are being used by the industry in various food categories. Table 1 provides indicative list of products in various food categories fortified by Omega-3 FAs sourced from fish, algae as well as plants.

Table 1. Omega -3 Fatty Acids fortified food products launched in various markets

Product category	Products lunched in the market
Fats & Spreads	Becel/Flora (Unilever, Canada), Fruit DOr (Unilever, France), Margarine with Omega 3 (Valle, Italy)
Milk & Other Dairy Drinks	Omega Plus Acticol (Nestlé, Singapore), Omega 3 Plus milk (Parmalat, Italy), Organic Whole Milk and Omega 3 (Stonyfield, USA), Future Star Kid Milk (Mengniu, China), Neilson Dairy Oh! (Saputo, Canada), Auchan Omega 3 Milk Drink (Alcampo, Spain)
Beverages and Juices	Enhanced Pomegranate Blueberry (Minute Maid, USA), Pure Premium Health Heart Orange Juice (Tropicana, USA), Recharge (Smartfish, Norway)
Cooking Oil	OlivExtra Plus (Pompeian, USA), Arawana 3A+ (Wilmar International, China), Nutrioli DHA (Ragasa, Mexico)
Breakfast cereals	Raisin Bran® Omega-3 from Flaxseed cereal (Kellogs, USA), Total® Plus Omega-3 (General Mills, USA)
Chewy/ Nutrition Bars	ALA Omega-3 Chocolatey Trail Mix (Kellogs, USA)
Infant food	DHA and Probiotic Rice Baby Cereal (Gerber, USA), Similac with OptiGRO™ (Abbott, USA)

Though refined anchovy oils are the largest category of Omega-3 oils in terms of volume (nearly 47% percent of the total oil volume in 2013), there is an industry trend for moving away from anchovy oils to higher-value products like krill oils, concentrates and algal oils. The market is experiencing a shift in focus from oils containing lower levels of EPA and DHA (such as 18:12 oils and cod liver oils) to the higher concentrates end of the market (> 60% EPA+DHA). Algal oils are preferred for infant formulas. Higher concentrates are being driven by the consumer need for smaller dosages and palatable formats (such as single shots, sachets, flavored gummies and chewables) as well as the need for the products to contain the right amount of EPA/DHA to achieve health claims.

III. Regulatory status of Omega-3 FAs:

Omega-3 FAs have numerous health approvals from various agencies resulting in increased demand for the product. The European Union (EU) has heart health claims approved with respect to Omega-3 FAs maintaining normal triglyceride levels and normal blood pressure. EU has also approved DHA claims for contributing to the maintenance of normal brain function and normal vision (European Commission, 2012). These claims are allowed for food which contains at least 40 mg of DHA per 100 g and per 100 Kcal and the EFSA daily recommended intake for Omega 3 FAs is 250mg/day. The Food and Drug Administration (FDA) has approved the claim of Omega-3 reducing the chances of coronary heart disease (CHD). The American Dietetic Association has recommended a minimum intake of 500 mg/day of EPA and DHA in order to have beneficial

health effects. The Institute of Medicine has set a Daily Value of ALA at 1,600mg/day, whereas no such level has been set for DHA and EPA.

The lack of recommended dietary intake (RDI) standard by FDA is considered as a challenge for the growth of the market over the next few years. In August 2014, EPA and DHA made the cut for a potential reference daily intake (DRI) review in the United States and Canada and was included for discussion in workshop in 2015. In November 2014, the Codex Committee on Nutrition and Foods for Special Dietary Uses approved a proposal to eventually establish a Nutrient Reference Value (NRV) for EPA and DHA. A NRV would represent a global recommended intake for these fatty acids, much like a dietary reference intake (DRI) value in the United States and the establishment of this RDI/NRV will result in further growth of Omega-3 FAs market.

IV. Sources of Omega-3 Fatty Acids

Depending on the source, Omega-3 FAs may occur as DHA or EPA as the predominant fatty acid or mixtures of DHA and EPA in varying combinations. Traditionally, fish oils from marine resources like anchovy or cod livers were the main source for EPA/DHA in combination. Some plants and algae are vegetarian sources that provide Omega-3 FAs. Algae are also the originating source of EPA and DHA in fish and krill, which obtain these fatty acids by feeding on algae. While algal oil provides EPA and DHA directly, plant sources like flaxseed and chia provide ALA which is the only Omega-3 FA in plants. The body must first convert ALA into EPA and DHA which is not always efficient.

Challenges with sources of Omega-3 FAs and the need for alternate sources

The major source of Omega-3 FAs in commerce is Anchovy fish oil. However, sustainability is a major challenge with marine supplies of Omega-3 FAs. Fish oils usage also pose challenges such as unpleasant odor, taste and poor oxidative stability (lower shelf-life). In addition, the unavoidable presence of EPA along with DHA, which is not acceptable in some applications and presence of contaminants in fish oils (mercury, PCBs, dioxins, arsenic) led industry to look for new sources of Omega-3 FAs other than fish oil. Bioavailability of Omega-3 FAs also influences the selection of source. Krill is increasingly becoming an important alternative source of Omega-3 FAs due to higher bioavailability.

With rise in vegetarianism, algae has become an attractive source for production of Omega-3 FAs. Omega-3 FAs from algal oils, however, face the challenge of higher prices compared to fish oil due to low economies of scale, high production and processing costs etc. This prevents the penetration of algal DHA among price sensitive market segments. Plant-based Omega-3 FAs, another vegetarian and sustainable option, are increasingly being used in several foods and beverages as they pose less problems of stability when compared to fish or algae oils. Grains like flaxseed, quinoa and chia provide a good choice for ALA (the only form of Omega -3 in plants) along with other nutrients like lignans, protein and fibre. However, conversion of ALA into EPA and DHA in the body is not always efficient.

Forms of Omega-3 and Bioavailability:

The form of the Omega-3 FAs affects their bioavailability and efficacy. The early generation of Omega-3 forms were triglycerides (TG), free fatty acids (FFAs), ethyl esters (EEs) and phospholipid forms. The new generation Omega-3 forms include glycolipids and Omega-3 salts (GOED, 2014). Some studies have shown that Omega-3 with polar lipids (phospholipids in krill oil and glycolipids in some algae) have the highest bioavailability. Similarly, the bioavailability of FFAs is higher than triglyceride and ester forms (FFAs > TGs > EEs forms). However, the triglyceride form is suitable for food and nutritional applications, as it is very stable and natural form.

In fish and most algal oils, the Omega-3 FAs are primarily conjugated to a triglyceride backbone, whereas in krill oil the fatty acids are largely conjugated to phospholipids and hence Krill oil has better bioavailability than the fish oil. Krill oil also contains nutrients like astaxanthin that enhance the stability of Omega-3 FAs. Recently, Qualitas Health has launched Almega PL which is the only Omega-3 ingredient on the market that contains both phospholipids and glycolipids. Qualitas performed a clinical trial⁴ comparing the absorption of Omega-3 FAs between the algal oil of *Nannochloropsis oculata* and krill oil. The results showed that the algal oil offered significantly higher absorption and bioavailability of EPA. Novotech Nutra has launched NovoOmega® Omega-3 powder in the calcium salt form. The Omega-3 salt forms are soluble and easily digestible forms and have great market potential in pharma and supplement applications due to higher absorption. However, there is need for greater research on understanding how the composition of the fatty acids affects the function of the Omega-3 FAs.

V. New developments in sources of Omega-3 Fatty Acids

The future Omega-3 markets will need new sources to meet the increasing demand from the food and pharma industry. Algae, a vegetarian source, provides much higher levels of Omega-3 FAs and do not contain contaminants such as mercury, PCBs and dioxins that could be found in marine sourced fish oils. Due to this reason, algae oils are only permitted in DHA fortification of infant formula in USA. Moreover, algae offers year round cultivation and can provide predictable yields. The type and proportion of Omega-3 FAs differs based on the species of algae. For example, *Cryptochodinium cohnii* produces only DHA whereas species such as *Nannochloropsis*, *Chaetocero* produce primarily EPA and some strains of *Schizochytrium* produce both DHA and EPA. In general, photosynthetic/ autotrophic algae produce higher levels of EPA and heterotrophic algae produce higher levels of DHA⁵. Algal based systems provide wider choice and make feasible the customizable product formulations by rebreeding of existing strains or blending of different strains grown together. Martek (now DSM) was the first to market EPA from algae in 2011 after it rebred its *Schizochytrium* strain to produce higher levels of both DHA and EPA. As a result, the company now offers Life's DHA and Life's Omega (DHA + EPA).

⁴ Kagan et al., 2013. Lipids Health Dis. 12: 102

⁵ Martins *et al.*, 2013 Marine Drugs 11: 2259-2281

i. Production technologies for algal source Omega-3 Fatty Acids:

New technological advances are overcoming the hurdles associated with algae cultivation and its processing and are helping algae reach its full potential as a source of Omega-3 FAs and other useful metabolites. Three types of systems are currently being used and researched for algae cultivation: fermentation (heterotrophic), open-pond cultivation (autotrophic) and photobioreactors (autotrophic - closed system). Commercially produced algal DHA today is predominantly from fermentation systems wherein sugars are used as energy source to grow algae in reactors. This process ensures ingredient is free from sea-borne contaminants/heavy metals. Leading suppliers like Martek (now DSM) have used fermentation system to produce DHA or DHA + EPA from *Cryptocodinium* and *Schizochytrium* species. Recently, Qualitas has launched a new algal oil in the market. Qualitas uses open ponds to cultivate the *Nannochloropsis* algae which naturally yields an oil with 30 % EPA and no DHA. Moreover, the oil contains Omega-3s bound to phospholipids and glycolipids, and hence it is a vegetarian alternative to krill oils. Table-2 highlights the various types of Omega-3 FAs produced by commercial suppliers using algal production systems.

Table 2. Algal strains and production systems adopted by commercial suppliers for Omega-3 FAs production

Company, (ingredient brand)	Algal Species	Production system	Type of Omega -3 FAs	Form of Omega -3 FAs
DSM/Martek (Life's DHA™)	<i>Cryptocodinium cohnii</i> <i>Schizochytrium sp</i>	Fermentation	DHA	Triglyceride
DSM (Life's Omega™)	<i>Schizochytrium sp</i>	Fermentation	EPA and DHA	Triglyceride
Lonza (DHAid™)	<i>Ulkenia sp</i>	Fermentation	DHA	Triglyceride
Kingdomway, China	<i>Schizochytrium sp</i>	Fermentation	DHA	Triglyceride
Source-Omega (Source Oil™)	<i>Schizochytrium sp</i>	Fermentation	DHA+EPA	Triglyceride
Qualitas Health (Almega PL™)	<i>Nannochloropsis oculata</i>	Open pond	EPA	Glycolipid and phospholipid structure

Source: Company websites, patents and regulatory applications

In an open-pond system, algae are grown in open ponds, tanks or containers using sunlight as energy source. Aurora Algae has developed an open-pond cultivation method that allows to grow algae using seawater. In contrast, Photobioreactor system is a closed system that provides control over conditions like sunlight exposure, temperature, and protection against contamination. Algae Biosciences plans to start commercial production using this system in 2015-16. Cellana has developed a proprietary ALDUO™ system, combining a series of photobioreactors (PBRs) with open ponds enabling economic and continuous production of diverse strains of microalgae. In the

autotrophic/ photosynthetic systems of culturing of algae, algal oils will also include other beneficial compounds such as phytosterols, chlorophyll, Vitamins C, D, and E, and the carotenoids. Table 2 provides a list of various other systems of algal production that are currently at pre-commercial stage. There are few technology developments by Indian companies like Avesthagen and ABL Biotechnologies Limited for algal based DHA production. However, there are no reports on commercial production of DHA by these players so far.

Table 3. Type of algal production systems for Omega-3 FAs that are at piloting phase / pre - commercial stage

Company (ingredient brand)	Algal Species	Production system	Type of Omega - 3 FAs
Aurora Algae (A2 EPA Pure™)	<i>Nannochloropsis sp</i>	Open pond, saline water	EPA
Butazyme	Heterotrophic algae	Fermentation	DHA+EPA
Fermentalg	<i>Schizochytrium</i>	Fermentation	DHA
Algisys	<i>Pythium irregulare</i>	Fermentation	EPA
Algae BioSciences (AlgaeBio Omega-3 Origins™)	Autotrophic algae	Photobioreactor	EPA + DHA (1:1 or customized)
BioProcess Algae	Autotrophic algae	Biofilms	EPA + DHA
Cellana (Renew™)	Autotrophic algae	Hybrid system (open ponds + photobioreactors)	EPA and DHA

Source: Company websites and patents

ii. New plant sources:

Plant sources like flax, chia continue to be popular choice for ALA. Recently, there is lot of interest in another Omega -3 FA i.e. Stearidonic Acid (SDA, C18:4, n-3) available from plant source. SDA is converted to EPA with higher efficiency when compared to ALA. Technology Crops International (TCI) has launched Ahiflower™ Oil, a proprietary branded form of *Buglossoides arvensis* seed oil, which is the richest natural plant source of SDA known. This oil contains both Omega - 3 and Omega- 6 fatty acids in combination.

Industry giants BASF, Cargill, Monsanto, Dow and DSM Nutritional Products are all set to bring to market Omega-3s sourced from agricultural sources, as is evident from these players announcing strategic partnerships to develop Genetically Modified crops with enhanced levels of Omega-3 FAs. BASF and Cargill announced a partnership in 2011 to develop a genetically modified form of canola that would yield a “next generation” canola oil containing EPA and DHA. Another canola variety being developed to yield DHA is in pipeline from Dow Agrosiences and DSM partnership. In 2013, DSM and Monsanto announced a partnership to deliver the first SDA Omega-3 soybean oil for use in foods in North America.

VI. New Processing Technologies for Omega-3 FAs:

Oils from various sources need to be extracted and/ or purified using chemical processes/ solvent based system. There is an increasing trend in using greener chemistry and avoiding harmful solvents in processing. Algae Biosciences uses a supercritical CO₂ extraction process as opposed to some players which employ hexane or other hydrocarbon-based solvents. Qualita's has entered into technology collaboration with Valicor Renewables for Algafrac™ technologies for the extraction and fractionation of algae oil. This technology provides scalable process for efficient and cost-effective extraction of polar and non-polar lipids. This hexane-free extraction keeps the natural and bioavailable polar-lipid Omega-3 form intact, while using significantly less energy compared to conventional dry oil extraction technologies. Novozymes is promoting enzymes (Lipozyme 435) as alternative to chemical processing of Omega-3 FAs. Enzyme-catalyzed esterification results in products of higher purity and creates less by-products than fish oils processed using chemicals. Moreover, the extraction occurs at low temperatures, thereby limiting the destruction of heat-labile components. Enzymes can also create new products with differing EPA & DHA ratios.

A proprietary chromatographic separation method developed by Equateq (acquired by BASF) enables to customize fatty acid concentrates with variable ratios of EPA and DHA at concentration levels of up to 99% purity. BASF's Crystalpure™ low temperature fractionation technology converts Omega -3 oils into pure, concentrated and natural triglyceride form, with no chemical manipulation. Croda's proprietary PureMax™ technology to concentrate and purify Omega-3 fish oil results in fish oil concentrates with high organoleptic and stability profiles. PureMax technology provides ultra-high vacuum and short residence times in order to maintain integrity of the oil and minimizes contaminants. Novotech Nutra has developed a process that converts Omega-3s into salts containing Calcium. The resulting salt form of DHA & EPA is soluble, easily digestible and has higher absorption.

VII. Stabilization technologies:

The Omega -3 FAs are highly unsaturated and susceptible to oxidation during all stages - procurement and handling, storing and processing. Use of sealed containers, low oxygen permeability and hermetically closed system during processing; nitrogen freezing and use of antioxidants during storage are some of the strategies for Omega-3 stabilization used by the industry. However, the high susceptibility of Omega -3 FAs to oxidation, taste and odor created challenges in adding Omega-3s to foods using traditional delivery methods. Microencapsulation and other stabilization technologies have helped overcome these challenges and have encouraged the development of shelf-stable products containing Omega-3 FAs like infant formulas, beverages and dairy products, baked foods etc. Some of these technologies adopted by commercial suppliers are listed in Table 4. Encapsulation involves entrapping an active component (e.g., a nutraceutical) within a secondary material, which may be referred to as the matrix or wall material. The

encapsulated active component is protected from the external environment until it is released by a trigger at a desired site and time. Ocean Nutrition's (now part of DSM) MEG-3 is stabilized with powder-loc microencapsulation technology which has significantly enhanced the ability of food manufacturers to use fish oil as a healthy food ingredient. This technology uses a double shell protection system to keep the EPA and DHA locked into the microcap while keeping the smell and taste of fish locked out of the food and beverage.

Cargill's IngreVita™ is a proprietary and stabilized blend of high oleic canola oil, Omega-3 FAs from fish oil and antioxidants, which is easy to use and sensory neutral. IngreVita™ oil can be stored at ambient temperature and used in wide range of food products. Similarly, Pizzey's Nutritionals has developed MeadowPure™ Omega 3 Ultra, a milled flaxseed and fish oil ingredient in which the fish oil is naturally encapsulated in the milled flaxseed. MeadowPure™ Omega 3 Ultra is shelf stable, has no taste or smell, and is easily incorporated into dry formulations. Cargill has also launched Clear Valley Omega-3 Oil that contains high stability ALA for incorporation in shelf stable foods.

Achieving Omega-3 stabilization provided opportunity for beverage applications that also require longer shelf-lives. Overcoming the challenges with shelf-life and stability have enabled the industry to focus on improving the palatability of encapsulated and liquid oils by developing deodorization technologies and offer unique products such as gummies and chewables that are appealing to consumers of all ages.

Table 4. Stabilization technologies adopted by commercial suppliers of Omega-3 Fatty Acids

Company (ingredient brand)	Stabilization technology
DSM/Martek (Life's DHA™)	Microencapsulation/ Spray-dried
Ocean Nutrition/ DSM) (MEG-3)	Powder-loc™ microencapsulation technology
Cargill (IngreVita™)	Blend of high oleic canola, EPA/ DHA from fish oil and antioxidants, Shelf life & storage at ambient temperature
InnoBio, China	Highly concentrated & encapsulated form
AnaBio Technologies	Microencapsulation system
Advanced BioNutrition	Microencapsulation (MicroMatrix™ technology)
Polaris Lipids	Stabilization against oxidation - Fish oil DHA 60 TG (QUALITYSILVER)
Croda (Ωmelife™)	Microencapsulation technology- concentrated Omega - 3 from fish oil, without the taste and smell
Biosearch Life (Eupoly-3®)	Emulsions and micro-encapsulated powder with special deodorization
Nu-Mega (HiDHA®, Driphorm®)	Microencapsulation/ Spray-dried powder

Wacker (OmegaDry®)	Cyclodextrin complexes for stabilizing omega oils against oxidation
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Source: Company websites and various other sources

VIII. Emulsions/ Solubilization of Omega-3 FAs

Adding Omega-3s to liquid products such as clear beverages and dairy was challenging and many companies have explored such beverage solutions. Emulsions are one of the important developments in Omega-3 formulations that have expanded their use in beverage applications, especially in clear beverages. SoluBlend has developed a technology to convert Omega-3 FAs into water-soluble ingredients. This technology results in transparent beverages with an improved shelf-life for the finished product, without adversely impacting taste, texture or appearance. The water-soluble Omega-3 FA concentrates does not have a typical oil-and-water phase separation when added to aqueous mediums. Similarly, Boreal's formulation technology transforms DHA oil into water soluble liposomal DHA, a homogeneous liquid that can be mixed in beverages without fishy odor. Aquanova's NovaSOLs technology can deliver a wide variety of active ingredients including Omega-3 FA in a stable, crystal-clear aqueous solution. The solubilizing system has a colloidal micelle structure, enabling an ultrafine distribution of active ingredients. Oceans Omega's water-soluble liquid emulsions technology has also helped expand the use of Omega-3 FAs, specifically within the beverage industry in non-refrigerated products such as waters, carbonated beverages, sports drinks, etc. The nanoparticle technology also delivers maximum bioavailability and minimizes cost. Croda has developed Incromega 3mulsion DHA, a highly concentrated, natural, fruit flavored emulsions that are convenient for sachet or syrup applications and ideal for delivering Omega-3 to children because they can get a full recommended daily intake in just one sachet or spoon serving.

Table 5. Emulsion/ Solubilization technologies adopted by commercial suppliers

Company (ingredient brand)	Emulsion/ Solubilization technology
Virun (OmegaH2O®)	Concentrated water soluble powders (Esolv® technology) with shelf stability and free of odor
Agel (Ω-3)	Suspension gel technology
Boreal Technologies	Liposomal technology for water soluble liquid formulations
SoluBlend Technologies	Water soluble functional ingredients
DSM	Freezable DHA emulsion for acidic based shelf stable drinks
Ocean's Omega/ Mycell Technologies (Omega Infusion)	Water-soluble liquid emulsions containing high-concentrations of Omega-3s, no fishy aftertaste
Novotech Nutraceuticals (NovoOmega®)	Calcium salts of triglyceride oils with higher Omega-3 contents and bioavailability, longer shelf life

Conclusion:

The beneficial health effects and the approved health claims of Omega-3 FAs have given rise to a growing global interest in using them in various food products. Sustainability of sources, the bioavailability of Omega-3 FAs forms and the options for customization of EPA/DHA are determining the food industry's sourcing choices for Omega-3 FAs. Technological advances are helping the food industry in extending Omega-3 FAs delivery options and formulating more products with better organoleptic properties and helping consumers gain access to Omega-3 FAs in everyday products. The establishment of recommended dietary intake standards for Omega-3 FAs in the coming days is expected to result in further growth of Omega-3 FAs applications in food industry.



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