Challenges for the Delivery of Long-Chain n-3 Fatty Acids in Functional Foods

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Abstract

Extensive research has shown that increased consumption of long-chain omega-3 polyunsaturated fatty acids (n-3 LCPUFAs), namely α-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA), may lower the risk of chronic diseases, such as heart disease, cancer, and arthritis. Given that Western diets are deficient in n-3 LCPUFAs, enrichment of food products is seen as an alternative for increasing the intake of these fatty acids. However, because of the high instability of these fatty acids to oxidative deterioration, enrichment of foods with n-3 LCPUFAs has been technically challenging. This review provides an overview of different technical approaches that have been taken to overcome oxidation-related problems. This review also looks at the challenges faced by health organizations, food manufacturers, and food scientists for the delivery of long-chain n-3 fatty acids in functional foods.

INTRODUCTION

Scientific progress over the past 100 years has allowed researchers to better understand the biological origin of disease and metabolism of food at the cellular level. The role of the vast majority of food components in disease prevention and health promotion is becoming clearer to scientists and consumers. Consumers now have some knowledge to select from a wide range of foods that either inherently contain health-enhancing functional ingredients or have those ingredients included via fortification. Subsequently, health promotion can take place either by increased consumption of foods already a part of the diet or by adding new substances to an individual's diet by changing habits. Moreover, with the understanding of the role of the bioactive components at the cellular level, a more specific recommended allowance in the diet can now be obtained (IFT 2005).

Positive health outcomes associated with consumption of oily fish have been known since the 1780s, when its use first began as a medicine to cure arthritis and rheumatism (Zuidam & Shimoni 2010). Since then, long-chain omega-3 polyunsaturated fatty acids (n-3 LCPUFAs), the bioactive ingredient in fish oil, have demonstrated health benefits in the areas of neural development in infants, cardiovascular diseases (CVDs), platelet aggregation, hypertension, hyperlipidemia, cancer, dementia, Alzheimer's disease, depression, and inflammation. Increased tissue levels of n-3 LCPUFAs at a population level are associated with reduced incidence of several chronic diseases responsible for the largest global portion of disease (Garg et al. 2006, Jacobsen et al. 2008). As a result, there has been phenomenal growth in both n-3 LCPUFA–enriched functional foods and supplements. Consumer awareness relating to the health benefits of n-3 LCPUFAs appears to be the highest in Australia and Spain. These countries are also the leading markets for omega-3-enriched products (McManus et al. 2011).

Most nutritional guidelines now include recommendations for increased intake of n-3 LCPUFAs for preventing CVD. However, the dietary intake of these fatty acids still remains low, particularly in Western countries. Nevertheless, delivering n-3 LCPUFAs into Western diets presents its own challenges. Taste acceptability of enriched foods (or the lack of), cultural reasons, economic reasons, and concerns about contamination with methyl mercury and organochlorides have been the main issues limiting the increase in n-3 consumption (Williams & Burdge 2006). In this review, we look at the challenges faced by health organizations, food manufacturers, and food scientists for the delivery of long-chain n-3 fatty acids in functional foods.

LONG-CHAIN OMEGA-3 POLYUNSATURATED FATTY ACIDS AND THEIR ROLE IN HUMAN HEALTH

Omega-3 or n-3 fatty acids are polyunsaturated fatty acids with a backbone of 18 to 22 carbon atoms in their chain. They contain more than one double bond, with the first one beginning at the third carbon atom. The first of the three main n-3 LCPUFAs is α-linolenic acid (ALA), with an 18-carbon-chain backbone and three double bonds. It is present in a wide variety of plant-based foods, such as soybean oil, rapeseed oil, walnuts, and green leafy vegetables (Holub 2002, Metcalf et al. 2003). The other two main n-3 LCPUFAs are the longer chain variants: eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), with a backbone of 20 and 22 carbon atoms and five and six double bonds, respectively, as illustrated in **Figure 1** (Kamal-Eldin & Yanishlieva 2002, McManus et al. 2011, Metcalf et al. 2003). EPA and DHA are found in high concentrations in oily fish, such as salmon, mackerel, anchovy, and other marine sources (**Table 1**) (He 2009).

All n-3 LCPUFAs are essential fatty acids in our diet because of the body's inability to synthesize these from other fatty acids consumed in the normal diet. Humans lack the desaturase enzyme that is typically responsible for inserting double bonds in saturated fatty acids, n-9 monounsaturated

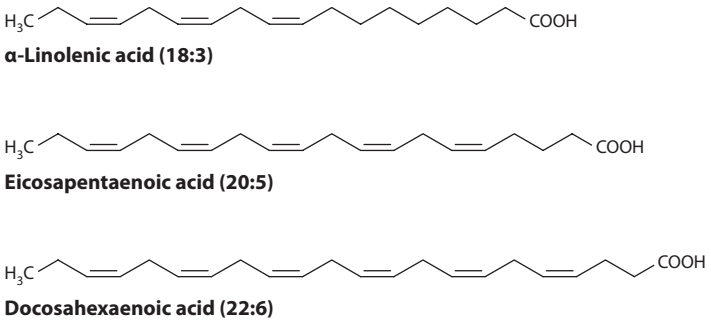

Figure 1

Chemical structure of the three main omega-3 long-chain polyunsaturated fatty acids (LCPUFAs).

fatty acids, or n-6 polyunsaturated fatty acids to convert them into n-3 LCPUFAs (Gebauer et al. 2006). ALA can be converted into EPA and DHA by the human body, but the rate of conversion has been limited for DHA. ALA to EPA conversion has been observed to be as high as 8%. It has been suggested that there may be a higher conversion rate of ALA into EPA and DHA during pregnancy (Williams & Burdge 2006).

CVD is the leading health problem in both developed and developing countries. Nearly twice as many deaths are caused in the developing countries by CVD as by HIV, malaria, and tuberculosis combined. Although the pattern of growth of CVD may be different in affluent countries compared with developing countries, the burden on economies in all countries continues to climb. In 2006, the direct and indirect costs relating to CVD in the United States alone were $400 billion. The

Table 1 Omega-3 fatty acid content of selected fish and plants

Source	EPA+DHA or ALA
Fish and seafood[a]	*mg 100 g*$^{-1}$
Anchovy	2,055
Atlantic salmon (farmed)	2,147
Herring	2,014
Atlantic salmon (wild)	1,840
Tuna (blue fin)	1,505
Mackerel	1,203
Trout (farmed)	875
Cod	158
Plant oils	*g 100 g*$^{-1}$
Flaxseed oil	53.3
Walnut oil	10.4
Rapeseed oil	9.138
Soybean oil	6.789
Rice bran oil	1.6
Avocado oil	0.957
Olive oil	0.761
Safflower oil	0.096

[a]Data related to cooked fish (USDA 2011).

situation is similar in many developing countries (Gaziano 2007). Well-controlled randomized clinical studies, such as the GISSI (Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico) study, have suggested that the consumption of high amounts of n-3 LCPUFAs resulted in an improvement in cardiovascular health in individuals with a history of myocardial infarction (Barrow et al. 2007, Williams & Burdge 2006). More recently, the Oxford Durham study showed improvement in the mental performance of school-aged children with high n-3 LCPUFA consumption (Barrow et al. 2007). A beneficial effect on the development of the visual system of preterm infants was also observed with the increased intake of n-3 LCPUFAs based on feeding trials (Williams & Burdge 2006). Being pleiotropic in nature, long-chain n-3 fatty acids are known to be involved in a wide variety of biological functions in the human body (Garg et al. 2006). Both n-6 and n-3 LCPUFAs are responsible for the flexibility of biological membranes and are also the precursors of eicosanoids. Eicosanoids are lipid mediators generated by the biological oxidation of polyunsaturated fatty acids [arachadonic acids (AA), EPA]. Eicosanoids include prostaglandins, thromboxanes, and leukotrienes, which exert profound biological effects in vivo, including inflammatory and immuno responses, and work as messengers in brain function (Funk 2001, O'Donnell et al. 2009). AA and linoleic acid (LA), the main n-6 fatty acids in the diet, compete with n-3 LCPUFAs (mainly EPA) for the same enzymes. Although the desaturase enzymes favor n-3 to n-6, a high LA intake would interfere with the desaturation and elongation of ALA (Simopoulos 2008).

Because Western diets consist primarily of n-6, which is derived mainly from refined cooking oils (corn, sunflower, etc.), the conversion of ALA to EPA is restricted. With the LA conversion to AA, a larger amount of AA can lead to higher production of eicosanoids, thereby changing the physiological state of the body to one that is prothrombotic and proaggregatory (Simopoulos 2008). It is therefore critical to maintain a proper n-3:n-6 balance, as these eicosanoids have an antagonistic function depending on their precursors (Garg et al. 2006). A ratio of 1:4 between n-3 and n-6 is recommended for prevention of CVD. The current ratio of n-3:n-6 in Western diets is estimated to be between 1:15 and 1:16.7 (He 2009, McManus et al. 2011).

The consumption of all three major n-3 LCPUFAs has been associated with reduced risk of CVD, but a large quantity of ALA has to be consumed to provide the health benefits (Metcalf et al. 2003). In normal diets, approximately 15 times more ALA has to be ingested to provide a similar function as EPA (Gebauer et al. 2006, Jacobsen et al. 2008).

RECOMMENDED INTAKE OF LONG-CHAIN OMEGA-3 POLYUNSATURATED FATTY ACIDS

It is evident that several health agencies worldwide recognize the importance of increasing EPA and DHA intake from fish to decrease the risk of CVD (Barrow et al. 2007). The dietary guidelines for Americans state that "evidence suggests consuming approximately two servings of fish per week (approximately 227 g) may reduce the risk of mortality from coronary heart disease (CHD) and that consuming EPA and DHA may reduce the risk of mortality from CVD in people who have already experienced a cardiac event" (Gebauer et al. 2006). Some of the recommendations for medical management of elevated blood triglycerides range from 2 to 4 g of EPA and DHA per day (Barrow et al. 2007). **Table 2** summarizes the recommended intakes from various organizations; these intakes range from 190 to 1,000 mg per day. To increase the consumption of fish in the Western diet, a major alteration in dietary habits would be warranted. The alternative approach suggested to consumers is through the consumption of fish oil supplements, which is inconvenient for many people. The only other suitable alternative would be to add n-3 LCPUFAs to a wide range of commercially available food products (Metcalf et al. 2003).

Table 2 A summary of the recommended intake from various organizations[a]

Source	Recommended daily dose of EPA + DHA (mg)	Population
National Health and Medical Research Council (Australian Nutrient Reference Values)	190	General population
British Nutrition Foundation Task Force	500–1,000	People at risk of cardiovascular diseases
U.K. Department of Health	200	General population
U.S. National Academies of Science, Institute of Medicine	200	General population
International Society for the Study of Fatty Acids	650	General population
American Heart Association	1,000 Oily fish (twice per week) >3 g d^{-1}	People at risk of cardiovascular diseases General population To reduce triglyceride levels
National Institutes of Health	300	Pregnant and lactating females

[a]Reproduced with permission from Garg et al. 2006.

Metcalf et al. (2003) demonstrated the incorporation of the recommended intake of n-3 LCPUFAs (200–400 mg) in the diet of subjects by fortification of everyday food with fish oil. They were also able to include one gram of n-3 LCPUFAs per day in diets of subjects with a history of CHD. A number of other studies have achieved a daily intake of one gram per day with fish oil fortification, but these studies have failed to take into account the overall sensory acceptability of these food products by subjects (Metcalf et al. 2003). Although addition of n-3 LCPUFAs into commonly consumed foods presents a very attractive opportunity, their oxidative instability makes it very difficult to protect these fatty acids from various environmental conditions. The oxidative instability of n-3 LCPUFAs is due to their high degree of unsaturation and cannot be easily overcome by the addition of natural antioxidants (Kamal-Eldin & Yanishlieva 2002). The mechanism of oxidation and the preventive strategies developed to date are discussed in the following sections.

OXIDATION PROCESSES IN LONG-CHAIN OMEGA-3 POLYUNSATURATED FATTY ACIDS

The principal technological challenge for the successful development of n-3 enriched foods is the prevention of lipid oxidation (Jacobsen et al. 2008). Because of the highly unsaturated nature of n-3 LCPUFAs, their susceptibility to oxidation is amplified. This process gives rise to rancidity and an extremely unacceptable fishy off-flavor (Taneja & Zhu 2006). The process of oxidation is initiated either by the presence of small amounts of free radicals, which are atoms with at least one unpaired electron, or light-activated photosensitizers. Either of the above mentioned are capable of subtracting a hydrogen atom from the methylene group situated between the double bonds, creating another free radical on the fatty acid molecule (**Figure 2)** (Ries 2009). This newly generated radical reacts with oxygen to form peroxyl radical and hydroperoxides in the propagation phase (Reactions *a* and *b*). The more the number of double bonds in the unsaturated fatty acids, the greater the variety of hydroperoxides produced. The hydroperoxide can further break down into an alkoxyl radical and a hydroxyl radical (Reaction *c*). The hydroperoxides can also react with metal ions (+II), resulting in the formation of alkoxyl radical and metal ion (+III) (Reaction *d*). This reaction then carries on with the conversion to metal ion (+III) and a peroxyl radical (Reaction *e*). Typically, this latter reaction is very fast, so to prevent it from taking place the oxygen

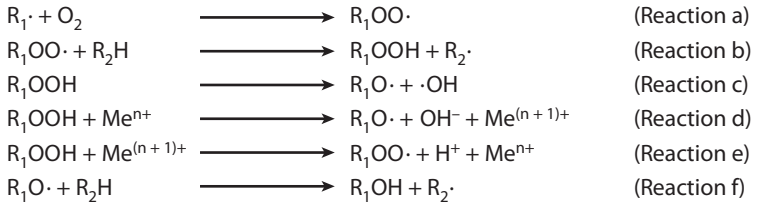

Figure 2

Principal reactions in the auto-oxidation of unsaturated fatty acids.

levels have to be very low. The reaction is terminated when two radicals react with each other to form a nonradical product. During the breakdown of the n-3 chain, aldehydes and ketones, which are secondary oxidation products, are generated. These are easily perceivable at very low concentrations and are mainly responsible for the unacceptable fishy off-flavor development (Ries 2009, Taneja & Zhu 2006).

Although the oxidation process in bulk oil and food systems is the same, the mechanisms of oxidation are somewhat different. Lipids in foods (such as milk, mayonnaise, salad dressings, margarine, soups, beverages, and desserts) are often present in the form of oil-in-water or water-in-oil emulsions. Oxidation is believed to take place at a faster rate in the food emulsion systems because of the presence of multiple phases. The possibility of oxidation taking place in the oil phase, in the aqueous phase, or at the interface makes the mechanisms very complex. Moreover, the effectiveness of antioxidants in such systems is very difficult to predict (Jacobsen 2008, Jacobsen et al. 2008, Waraho et al. 2011). The most important drivers of oxidation are metal ions, especially iron, which are present in trace amounts in most foods. Food emulsions have the aqueous and oil phase separated by an interface that comprises amphiphilic molecules (emulsifiers or surfactants). Transition metals, such as iron, promote oxidation by preferentially residing at the interface and decomposing lipid hydroperoxides. Factors affecting the rate of such reactions include the electrical charge on the droplet surface, the thickness of the interfacial layer, the presence of other components in the emulsion (such as protein and polysaccharides), types and concentrations of antioxidants present, and dissolved oxygen concentration.

CONTROL OF OXIDATION USING ANTIOXIDANTS

Antioxidants are commonly used by the industry to stabilize marine oils intended for use in food and pharmaceutical products. Antioxidants can be natural or synthetic. Because of their low cost, synthetic antioxidants have been widely used; these include butylated hydroxytoluene (BHT), butylated hydroxyanisole (BHA), tertiary butyl hydroquinone (TBHQ), and gallates. However, negative perception and safety concerns about synthetic antioxidants have led to an increased interest in natural antioxidants. Some common natural antioxidants include tocopherols, rosemary extract, and green tea extract. Mixtures of tocopherols, lecithin, and ascorbyl palmitate are commercially available and show synergistic function in antioxidative activity. This mixture also appears to provide protection against thermal deterioration during oil processing (Jacobsen 2010).

Antioxidants are used in bulk oils to prevent oxidation by scavenging free radicals and inactivating pro-oxidants, as the oil refining process cannot get rid of all the trace pro-oxidants. In food systems, the reactivity of these antioxidants can increase or decrease as a result of interactions with other compounds present in the food system (Waraho et al. 2011). Moreover, the effects of the same antioxidant were observed to be different in different food matrices. Certain antioxidants can be very potent in preventing oxidation in certain foods but might act as pro-oxidants in others.

Factors affecting the efficacy of antioxidants in food systems are the quality of the n-3 fish oil, the concentration of metal ions, pH of foods, and the types and concentrations of antioxidants used. Therefore, systematic compatibility of antioxidants needs to be tested on a matrix-by-matrix basis (Jacobsen 2010, Kamal-Eldin & Yanishlieva 2002).

DELIVERING LONG-CHAIN OMEGA-3 POLYUNSATURATED FATTY ACIDS IN FOODS THROUGH MICROENCAPSULATION

Fortification of commonly consumed food products with n-3 LCPUFAs is considered an innovative way of providing the health benefits to people without major alteration in their dietary habits (Garg et al. 2006). Shorter shelf-life products, such as bakery, dairy, or frozen food products, have been fortified using high quality fish oils (peroxide value of 0.5 meq kg^{-1} of oil or less). However, the amounts delivered (mg of n-3 LCPUFAs per serving) have been low. For applications such as cereals and long shelf-life products, even the best quality oils oxidize readily (Willumsen 2006). This is because some of the initiators and catalysts of the oxidation process are unavoidable during food processing and storage; it becomes extremely difficult to stabilize n-3-containing oils in such food systems for longer durations. Moreover, adding antioxidants to scavenge free radicals or oxygen or to chelate metal ions might not retard or inhibit oxidation because of the complex environment inside the food system (Jacobsen 2008). One way of protecting these oils in foods is by encapsulating them in a matrix that acts as a barrier, reducing the contact between the unsaturated fatty acids in the oil and oxidizing agents, such as light, heat, and metal ions (Ye et al. 2009).

Objectives of Microencapsulation

Microencapsulation technologies have been used in the pharmaceutical industry to stabilize various sensitive ingredients. With the increasing interest in functional foods, some of these technologies have been utilized in the food industry as well (Garg et al. 2006). Many bioactive components that were considered technically unfeasible to include in most matrices can now be microencapsulated (Gharsallaoui et al. 2007). Microencapsulation is a process in which small particles of the active and/or sensitive component (fish oil in this case), known as the core, are packaged within an encapsulating matrix (Desai & Park 2005).

Microencapsulation can be used to stabilize n-3 oils against photo-oxidation and free radical–driven oxidation leading to organoleptically acceptable products. However, the human threshold for detection of the oxidized off-flavors is very low. Aldehydes, such as c-4-heptenal, t,c-3,6-nonadienal, and t,c-2,6-nonadienal, formed after oxidation of fish oil can be detected at a concentration of 0.04 ppm, 0.01 ppm, and 0.01 ppm, respectively. Thus, the technique used for microencapsulation must be very effective in preventing the formation of even very low levels of oxidation by-products (Barrow et al. 2007, Drusch & Berg 2008).

A comparison of various microencapsulation techniques available to the food industry to facilitate incorporation of n-3 LCPUFAs into foods as a function of their complexity and production capacity is illustrated in **Figure 3**. The main objectives of microencapsulation of n-3 LCPUFAs are as follows (Drusch & Mannino 2009, McClements et al. 2007):

1. To enhance stability of the encapsulated n-3 LCPUFAs during storage before being added to food.
2. To be compatible with the food matrix and prevent oxidation of n-3 LCPUFAs with no effect on taste, texture, or shelf life of the food product.
3. To be readily degradable in the gastrointestinal tract upon consumption to release n-3 LCPUFAs for absorption.

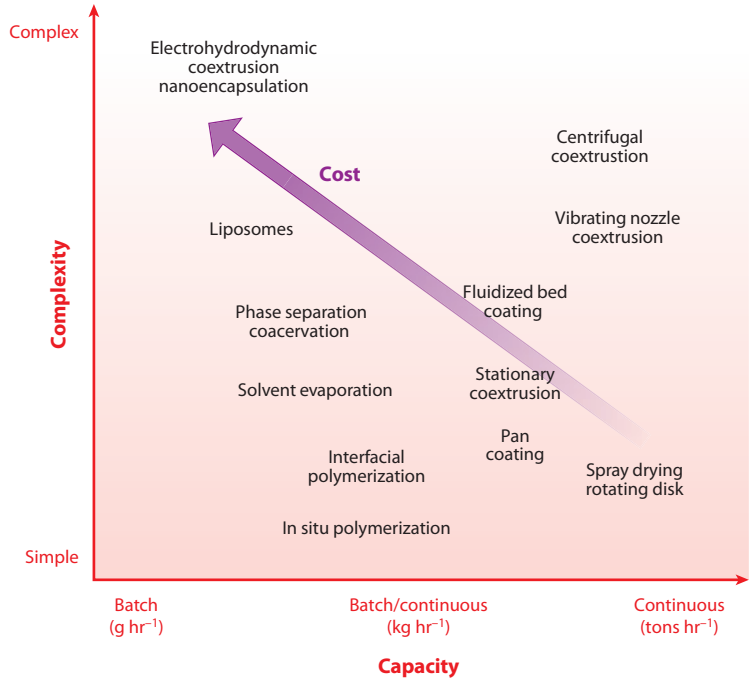

Figure 3

Relative complexity, capacity, and cost of various microencapsulation processes. Adapted with permission from SwRI (2011).

The stability of the microencapsulated ingredient depends on how well the core has been stabilized. Also, the robustness of the carrier matrix plays a major part in keeping these ingredients stable during various processing conditions (Drusch & Mannino 2009). The stability of the microencapsulated ingredient requires a balance of antioxidant and chelators in order to survive the processing and subsequent storage. Also, an alternative approach has been suggested because a single microencapsulated n-3 LCPUFA ingredient might not be able to stabilize the oil in all food matrices. It was suggested that the suitability of a microencapsulated n-3 LCPUFA ingredient to a certain food matrix environment must be evaluated first, then alteration should be made to improve suitability of the n-3 ingredient to the food matrix (Ubbink & Kruger 2006).

Overview of Microencapsulation Techniques

Various techniques are now available for the food industry to achieve efficient microencapsulation using different types of food-grade encapsulating and stabilizing materials as coating material (**Table 3**). The selections of the coating material and the technique are made independently, with the goal being to maximize stability of the core (Desai & Park 2005). In some processes, the selection of the wall material involves trial and error followed by the evaluation of the efficiency of the microencapsulation process. The stability of the formed microcapsules is evaluated under different storage conditions (Beindorff & Zuidam 2010).

An important requirement for most microencapsulation techniques is that they produce particles that are soluble in water for ease of handling. However, this is cause for concern because storage stability at high humidity can cause off-flavor development due to leakage of core material.

Table 3 Commercially available n-3 ingredients[a]

Supplier	Trade name	Technology
Arjuna, India	Zepufa	Spray-dried powder with starch as the oil dispersion medium
BASF, Germany	Dry n-3	Spray-dried matrix containing gelatin and sucrose coated with starch
Croda, United Kingdom	Omelife	Milk protein–based oil-in-water emulsion containing antioxidants
DSM, The Netherlands	Ropufa	Spray-dried powder with gelatin and sucrose matrix coated with starch
The Wright Group, United States	Supercoat omega-3	Spray-dried modified starch and corn syrup solids containing matrix
Nu-Mega, Australia	Driphorm	Spray-dried powder made with Maillard reaction products
Wacker, Germany	OmegaDry	Molecular inclusion complexes using γ-cyclodextrins dissolved in water followed by drying
Ocean Nutrition Canada, Canada	Meg-3 Calshell	Multishell complex coacervate of gelatin and polyphosphate followed by spray drying
Denomega, Norway	Denomega GAT 100	Calcium alginate microspheres

[a]Adapted from Barrow et al. 2007, Beindorff & Zuidam 2010, Desai & Park 2005, and Drusch & Mannino 2009.

Some microencapsulation processes produce water insoluble microparticles that present some advantages, but their bioavailability has been questioned because they do not disintegrate readily in the gastrointestinal tract (Beindorff & Zuidam 2010). Furthermore, having a continuous process for microencapsulation is advantageous because it reduces processing time and lowers product losses due to shut down and start up in a commercial setup (Tan et al. 2009). The following section gives a brief description of the main microencapsulation techniques currently used to stabilize n-3 LCPUFAs.

Emulsion-based delivery systems. Emulsion systems can be oil-in-water or water-in-oil, or more complex oil-in-water-in-oil or water-in-oil-in-water emulsions. Emulsifiers and stabilizers are commonly used to produce stable emulsions (McClements 2010). Particle size distribution, droplet charge, and interfacial thickness are some of the important characteristics of an emulsion system that affect its encapsulation efficiency and stability over time. More recently, modification of the interfacial characteristics has been considered one of the most powerful tools in the design of n-3 delivery systems. This has been done by selection of specific emulsifier/stabilizer types and then alteration of the system composition or processing conditions to provide special functionality (McClements et al. 2007).

The electrical properties of the interfacial layer may influence the oxidative stability in emulsions. Pro-oxidant metal ions in the aqueous phase are attracted toward the oppositely charged surface of the droplet. Surfactants [such as lecithin and diacetyl tartaric (acid) ester of monoglyceride] and polysaccharide emulsifiers (such as gums and modified starches) produce emulsion droplets that have negatively charged surfaces; these droplets may attract metal ions and promote oxidation at the interface (McClements et al. 2007, Zuidam & Shimoni 2010). Droplets stabilized by a positively charged emulsifier may repel metal ions (such as iron), reducing

oxidation (Beindorff & Zuidam 2010). Mei et al. (1998) made corn oil-in-water emulsions using a negatively charged emulsifier (sodium dodecyl sulphate), an uncharged emulsifier (Brij 35), and a positively charged emulsifier (dodecyltrimethylammonium bromide). The emulsions containing a positively charged emulsifier and the uncharged emulsifier showed much slower oxidation rates than the emulsions made using the negatively charged emulsifier.

Given that low-molecular-weight, positively charged emulsifiers are not commonly found in manufactured foods, it has been suggested that milk proteins, under acidic conditions (lactoferrin at neutral pH), could be a better alternative. Salmon oil-in-water emulsions stabilized by whey protein isolate were studied by Hu and coworkers (2003); they found that the oxidative stability of such emulsions was the highest at pH 3, presumably because of the positively charged interface, thus repelling metal ions away from the emulsion droplets (Hu et al. 2003). However, in another study the same group also found that the interfacial charge might not be the only factor responsible for slower oxidation rates. It was reported that whey proteins are able to inhibit lipid oxidation through a combination of free radical scavenging by free sulphydryl groups and chelation of pro-oxidant metal ions (Faraji et al. 2004). This property of milk proteins to chelate metal ions was found to be very important. Caseins (from sodium caseinate) are known to have superior stabilizing abilities because of their disordered and substantially hydrophobic structure (Faraji et al. 2004). Owing to the high content of phosphoseryl residues, caseins exhibit a specific metal-binding ability that in turn inhibits lipid oxidation (Singh 2011). Moreover, only a fraction of the proteins adsorb at the oil droplet interface during emulsification. It was reported that excess whey protein in the continuous phase may inhibit lipid oxidation in oil-in-water emulsions. The free-radical scavenging and metal-chelating activity of whey proteins can be enhanced by thermal treatment, which exposes the sulphydryl groups normally hidden in the interior of the molecule (Waraho et al. 2011).

A patent by Singh and colleagues (2006) exploited the antioxidant ability of milk proteins by stabilizing fish oil (30 wt %) using a mixture of whey protein and caseinate (Singh 2011, Singh et al. 2006). The inventors showed that mild heat treatment (90°C for 5 min) caused the globular whey proteins to expose their sulphydryl groups, which underwent a sulphydryl-disulphide interchange reaction, resulting in complex formation between the caseinate and whey proteins. The resulting emulsion provided greater physical stability and lower oxidation levels than the emulsions formed with individual milk proteins or an uncomplexed mixture of proteins (Singh et al. 2006). This novel emulsion technology was commercialized, and the products are sold by Croda International Plc (United Kingdom–based fish oil manufacturers) under the brand name Omelife^{TM}. The inventors used a processed cheese model system to investigate the effects of processing and storage on the oxidative stability and sensory properties in food products fortified with the patented fish oil emulsion. The processed cheese fortified with fish oil emulsion was compared with a similar cheese product containing an equivalent amount (50 g kg^{-1}) of fish oil added directly. Data were gathered on primary and secondary indicators of oxidation over 40 days of storage at 30°C. The results showed that fortification through fish oil emulsion resulted in lower oxidation rates than direct fish oil fortification over the tested storage period. The sensory quality of the processed cheese fortified with fish oil emulsion was also found to be higher compared with direct fish oil fortified cheese over a range (5–40 g kg^{-1}) of fish oil addition levels (Ye et al. 2009).

Because emulsion-based delivery systems are heterogeneous in nature, it is possible to develop novel strategies for controlling the stability of n-3 LCPUFAs at various regions of the emulsion. For instance, addition of water-soluble antioxidants, such as chelators, can be added to the aqueous phase, and the droplet interface could be engineered to inhibit lipid oxidation (McClements et al. 2007). Emulsions are easier to disperse into water-based foods, such as beverages and dairy products (Djordjevic et al. 2004). Another advantage of emulsion-based systems is

that they can be created from food-grade materials using the standard unit operation employed by the food industry. Moreover, the rheological properties of emulsions can be modified by changing their composition and processing parameter for suitability in specific applications (McClements et al. 2007). However, most emulsions are prone to instability with the change in pH, mineral concentration, and environmental stresses, such as heating and freezing. Also, because of the limited number of emulsifiers available to form stable interfacial layers, the range of protection against oxidation has been limited (McClements et al. 2007). Commercially, emulsions are expensive to ship and store as they contain a large percentage of water. To reduce the packaging and storage requirements, the emulsions are generally dehydrated to transform them into dry powders. Powders are easier to handle and have a longer shelf life (Vega & Roos 2006). The following sections give details on spray drying to microencapsulate n-3 LCPUFA–containing oils.

Spray drying. Spray drying involves atomization of the feed (dispersion or emulsion) using a pressure nozzle or a centrifugal wheel into hot medium (typically air), resulting in rapid evaporation of water (Vega & Roos 2006, Zuidam & Shimoni 2010). Depending upon the feed composition, dryer design, and operating parameters, spray drying can result in powder particles or agglomerate-type conformations (Beindorff & Zuidam 2010).

The powder particles obtained after spray drying an oil-in-water emulsion generally have a matrix-type structure in which the oil droplets are embedded in a continuous phase of wall material and carrier material (Jafari et al. 2008). Most commonly used wall materials for microencapsulation by spray drying include gums (gum arabic, locust bean gum), lipids (wax, palm fat), proteins (gelatin, milk proteins, soy protein), polysaccharides (starch, xanthan, pullulan, guar gum, alginate), and mono-, di-, and oligosaccharides (hydrolyzed starch, lactose), as well as cellulose and its derivatives (carboxymethylcellulose, methylcellulose) (Drusch et al. 2007). Maltodextrin, glucose syrup, modified starch, sugars, and/or modified cellulose can be used as carrier material (Beindorff & Zuidam 2010).

Under appropriate handling and storage conditions, the physicochemical properties of spray-dried powders are dictated by the composition of the particle surface. Properties like flowability and redispersion are directly associated with the amount of free oil on the surface of the powder. Most importantly, in the case of powders containing fish oil, any free oil is available for oxidation and may lead to off-flavor development (Drusch & Berg 2008, Keogh et al. 2001, Kim et al. 2002).

Fluidized bed coating subsequent to spray drying has been used to provide a second coating on the surface of the dried particles by using materials such as starches, waxes, maltodextrin, and gums (Drusch & Mannino 2009). Modification to nozzle and spray-drier design has also led to the highly efficient coating capabilities by simultaneously allowing feed, hot air, and a second coating material in the drier (Drusch & Mannino 2009). For example, DSM N.V.'s (a global ingredients manufacturer in the health and nutrition sector) Ropufa fish oil powder for infant formula uses fish gelatin and sucrose as wall materials that are later spray dried and coated with cornstarch to improve dispersability. Another commercial product that uses spray drying for microencapsulation is manufactured by Nu-Mega Ingredients Pty. Ltd. (Australia). In this, milk proteins and lactose act as wall materials. The patent describes the preparation of glycated proteins (via heating for 30–90 min) to impart antioxidative properties that are then blended with fish oil and spray dried with an optional coating of wax or starch (Jin et al. 2008, Drusch & Mannino 2009).

A second coating may improve flow properties and redispersion behavior to a certain extent by reducing oil on the surface but may not necessarily prevent off-flavor development during spray drying (Drusch & Mannino 2009). Extensive studies have shown that surface free-oil coverage can be minimized by optimization of the composition of the powder, protein-to-oil ratio, atomization

and drying parameters, viscosity, and storage conditions (Faldt & Bergenstahl 1995, Bergenstahl 1996, Faldt et al. 1993, Hogan et al. 2003, Kim et al. 2008). However, a comprehensive understanding of the mechanisms behind surface formation and composition in emulsion powders still needs to be attained (Kim et al. 2008, Vega & Roos 2006).

Microencapsulation using spray drying also has some disadvantages. Firstly, the wall material or the coating used to encapsulate has to be water-soluble and preferably have high solubility. Therefore, only a very few coating materials are available for the encapsulation of n-3 LCPUFAs. Secondly, the porous structure and high surface area make the spray-dried powders highly susceptible to oxidation due to air exposure. However, shelf life has been shown to be enhanced by packaging spray-dried powders in multilayered foil packs flushed with nitrogen gas (Beindorff & Zuidam 2010). Lastly, spray-dried powders have low oil loading (Drusch & Mannino 2009). Although spray-dried powders have been successful in products such as bread and some other short shelf-life baked products, their stability in long shelf-life products remains poor (Barrow et al. 2007).

Complex coacervation. In a system with two colloids, the separation of the colloids having opposite charges has been named complex coacervation (de Kruif et al. 2004). This method can be used to deposit multiple layers of polymers on the core material (Drusch & Mannino 2009). One such method has been described in the patent by Yan and coworkers (2004); the process begins with the formation of an emulsion with a solution of a positively charged polymer, such as gelatin type A (isoelectric point of 9) or chitosan and fish oil. A second solution made with a negatively charged polymer, such as sodium polyphosphate, gelatin type B, gum arabic, alginate, or carboxymethylcellulose, is added to the emulsion. The pH of the emulsion is adjusted, resulting in the coacervates with the polymers precipitating on the core, giving it enhanced stability. The size of these microparticles is typically 1–5 μm. These microcapsules can be agglomerated by agitation while cooling, which may be followed by addition of a cross-linking agent (gluteraldehyde or transglutaminase) to strengthen the shell. This is followed by washing with water and spray drying to remove moisture. The final powder is free flowing with a particle size of 10–100 μm and may have oil loading of 40% to 90% (Beindorff & Zuidam 2010, Drusch & Mannino 2009, Yan et al. 2004).

The main advantage of complex coacervation over simple spray drying is the higher oil content and the relatively low amount of surface oil. Surface oil content in the produced coacervates is about 0.2% of the total oil, as compared with 0.2% to 1.0% in spray-dried powders (Barrow et al. 2007). Higher amounts of surface oil are thought to be directly proportional to unencapsulated oil on the surface available for oxidation, given that ample concentration of oxidation initiators are available in the environment (Jafari et al. 2008). The main disadvantage of complex coacervation is the use of gelatin in the process, which makes it difficult to acquire halal or kosher status because it is obtained from pig skin (Barrow et al. 2007, Beindorff & Zuidam 2010). Other sources of gelatin (beef, poultry, and fish) are available but are not very cost effective (Beindorff & Zuidam 2010). The process is also thought to be quite complex, as meticulous control over processing parameters is required throughout the process and can be rather expensive. Also, the use of gluteraldehyde as a cross-linking agent has strict legislation in some countries, and therefore its concentration has to be carefully monitored (Desai & Park 2005).

Alginate-based microspheres. Alginate-based microspheres are widely used in the pharmaceutical and medical fields (Sainz Vidal et al. 2003). More recently, alginates have been used to encapsulate biomaterials, such as probiotic bacteria, functional oils, and those in other controlled delivery applications (Hoad et al. 2011). Derived from brown algae, alginates are generally

regarded as nontoxic and biocompatible (Tan et al. 2009). Alginates are block copolymers composed of β-D-mannuronic acid and linked with 1–4 linkages. Calcium is commonly used to start ionic interaction between α-L-guluronic acid residue to form chains of two or more units, causing gel formation (Hoad et al. 2011, Zhang et al. 2006). Alginates, being ionic biopolymers, exhibit pH and charge sensitivity that offers encapsulation opportunities (Hoad et al. 2011). There are several methods used to produce microspheres, depending on the release of calcium ions to cause gelation. One such method involves the preparation of a water-in-oil emulsion in which the calcium ions are present in the water phase. Calcium alginate solution is then added to this emulsion, which causes the alginate to deposit on the surface of the droplets because of phase inversion (Casana Giner et al. 2006).

Another method involves the use of an oil-in-water emulsion made with alginate, an emulsifier, and a second surfactant sprayed into calcium chloride solution. These particles are dried after being collected and washed to remove excess oil on the surface (Drusch & Mannino 2009). Further coating, hot air drying, and cross linking may be applied to enhance the barrier properties of the alginate microspheres (Zuidam & Shimoni 2010). Being relatively inexpensive, readily available, and safe to use in food products allows alginates to be common in the food and pharmaceutical industries (Tan et al. 2009). At the lab scale, microcapsule or bead systems are relatively easy to prepare using various available biopolymers, often resulting in high loading of core material in the final product. However, scaling up has proven to be very difficult and expensive because of the process being limited by small-sized batches (Anal & Singh 2007, Tan et al. 2009). In addition, the final matrix of the bead systems tends to be extremely porous, allowing diffusion of water in and out of the matrix (Anal & Singh 2007).

Other technologies. Mechanical processes, such as extrusion, are frequently used to stabilize sensitive core materials, such as flavors, in a glassy carbohydrate matrix with the primary objective of protecting the core from oxidation (Madene et al. 2006). These matrices are known to have very good barrier properties, and extruded particles are less porous than spray-dried particles, as no water is required (Drusch & Mannino 2009, Madene et al. 2006). Submerged coextrusion, a variation of the conventional extrusion process, involves the oil droplets being dropped simultaneously with a shell material (gelatin or other polysaccharides and a plasticizer) through a concentric vibrating nozzle in a stream of cooling oil. The cooling oil causes the hardening of the outer shell of the microparticles, which are then carried through for filtration and harvest. A second coating may also be applied to aid formulation and handling (Beindorff & Zuidam 2010, Dekker & Husken 2010, Zuidam & Shimoni 2010).

A method described in the patent by Dekker & Husker (2010) gives details of submerged coextrusion used for microencapsulation of fish oil. Gelatin was used as wall material, and glycerol was used as plasticizer. A wall material solution was first prepared by mixing gelatin (25% w/w) and water. Glycerol was added to this solution and heated to 80°C and subsequently cooled to 45°C. A coextrusion nozzle was used to feed the two streams simultaneously, i.e., fish oil was sent through the inner nozzle and gelatin solution was sent through the outer nozzle. The nozzle was connected to an oscillator for controlled vibration production, which aids in droplet breakage. The nozzle head was submerged in cooled vegetable oil at 14°C, which caused the gelatin to set on contact. The formed microcapsules were filtered and centrifuged to remove excess oil. This was followed by air drying. A second coating was applied to aid formulation and handling.

Melt injection is another mechanical process used to microencapsulate fish oil by using sugars around the core droplet to create a glass barrier that is impermeable to oxygen. The process involves blending of fish oil with antioxidants, emulsifiers, and water and then heating them to 100°C to solubilize all the sugars. For size reduction, this mixture is passed through a filter

followed by dropping into a pool of cold solvent that creates solid microparticles. The solvent also aids in removing any unencapsulated oil (Valentinotti et al. 2006). One of the main disadvantages of the melt injection process is the vulnerability of the microparticle to fluctuation of humidity, which leads to loss of particle quality. Also, the oil loading is limited to 10% to 20%. However, this process yields very stable particles that have a long shelf life if the storage temperature and humidity are well controlled (Beindorff & Zuidam 2010).

Calcium carbonate is abundantly found as the inorganic component in the shells of marine life and limestone (Ogomi et al. 2005). Being relatively cheap and environmentally benign in nature, calcium carbonate has been shown to form a microcapsule wall using a relatively simple technique. It is also suggested to improve rigidity of the shell and provide resistance to deformation due to heat (Long et al. 2010). The encapsulation of fish oil using calcium carbonate starts with the use of an anionic surfactant (such as sodium dodecyl sulfate) for emulsification of the oil. The calcium carbonate particles, when added to the emulsion while stirring, are electrostatically adsorbed on the surface of the oil droplets. The resulting solution could be spray dried or freeze dried. Calcium carbonate dissolves at low pH once the capsules reach the stomach. The oil loading of the capsules is similar to spray-dried powders; however, to make up for the costly processing, the capsules usually have high temperature and pressure resistance (Beindorff & Zuidam 2010).

A number of encapsulation processes using cyclodextrins have been described. These processes involve the dissolution of cyclodextrin in water and then further mixing of the core material in the solution. Crystallized molecules are then separated and dried into powder form (Desai & Park 2005). The main difference in these processes is the amount of water added to dissolve the cyclodextrin molecules (Madene et al. 2006). The process that uses kneading of cyclodextrin with minimal amounts of water has been suggested as being the most commercially practical out of the three, as very little water has to be removed by drying (Madene et al. 2006). The main function of cyclodextrins is believed to be in reducing off-flavor in n-3 LCPUFAs by means of complexation (Desai & Park 2005). Fish oil containing γ-cyclodextrins has been shown to resist oxidation for up to 24 h upon storage at 100°C (Beindorff & Zuidam 2010). One of the main disadvantages of the process is the low amount of oil loading, which is usually between 5% and 15% (Zuidam & Shimoni 2010). The use of cyclodextrins in food application is limited because of regulatory requirements in a number of countries and the high cost of the ingredient itself (Desai & Park 2005, Madene et al. 2006).

PACKAGING

It is well known that by minimizing the exposure of n-3 LCPUFAs to air, light metal ions, and high temperatures, oxidative stability can be improved in both oils and enriched foods. However, many of the modern packaging materials allow the consumer to see the actual product. In the case of omega-3 enriched food products, the use of foil packaging film or dark glass/plastic bottles has been found to be very useful in increasing the shelf life (Kamal-Eldin & Yanishlieva 2002).

Oil is known to dissolve five times more oxygen than does water. Thus, another approach to prevent oxidative deterioration is to remove oxygen during processing and packaging. Fish oil is shipped around the world, predominantly in low-oxygen-permeable packaging material with an inert gas purged through the oil phase and filled in the headspace to enhance stability. The difficulty with removal of oxygen is that less than 1% residual oxygen is very difficult to achieve in a commercial environment. Also, removal of oxygen is highly dependent on the food matrix. Multiple layers in packaging films and other materials with less permeability to oxygen are now generally used (Jacobsen 2008).

BARRIERS TO MEETING RECOMMENDED INTAKE OF LONG-CHAIN OMEGA-3 POLYUNSATURATED FATTY ACIDS AND REACHING MARKET GROWTH FORECAST

Because of the growing interest in health and wellness in the past two decades, the n-3 LCPUFA supplements market was estimated at $600 million in the United States alone in 2008. This was a 29% increase from 2007, and it was projected that the sales would increase 30% each year. The percentage of people in the United States who take fish oil supplements has jumped to 17% in 2011 from 8% in 2006 (Marketwire 2011). The enriched food market was worth $2 billion in 2007 in the United States, which included all three major n-3 LCPUFAs. This was expected to grow to $7 billion by 2011. In 2007, 723 new products enriched with n-3 LCPUFAs were launched in Europe, up from 291 in 2005 (Mellintin 2008, Starling 2008). However, since then only a handful of these new products achieved big sales. The two noteworthy products are a milk beverage in Spain and a bread in Australia (Barrow et al. 2007, Mellintin 2009).

There are a number of obstacles preventing the growth of n-3 enriched foods. The issue of contamination of fish has been recognized by the FDA. Methylmercury (MM), a heavy metal toxin, is found in different types of fish and is associated with neurological damage in fetuses and infants. However, the health benefits of eating fish outweigh the potential risks associated with contaminants (He 2009). The warning issued by the FDA was particularly aimed at limiting the exposure of the human fetus to mercury, which has been found in high concentrations in certain types of fish (He 2009).

Another challenge is the formulation of longer shelf-life complex food systems. Although a trial-and-error approach is usually successful in some simple food systems, such as dehydrated and frozen foods, the inclusion of n-3 fails miserably in complex food matrices in which a large number of physical, chemical, and biological factors influence the performance of active ingredients. Shelf-stable beverages and chilled meals are good examples of complex food matrices. Tight price margins and strict regulations pose further challenges (Ubbink & Kruger 2006).

It is unfortunate that a bioactive ingredient like n-3 LCPUFAs, which is a key nutrient for human health, is seeing a decline in the number of new products being introduced in the functional foods segment worldwide even though modern diets are seriously deficient. The fact that consumers are not able to see or feel the immediate health benefits of consuming n-3 LCPUFAs is the main reason why the n-3 LCPUFA-enriched foods market is seeing negative growth (Mellintin 2008, 2009). Off-flavor problems limit omega-3-enriched food products to 100 mg of EPA/DHA per serving. To meet the recommended daily intake, consumers must eat four to five servings, which is difficult to achieve (Mellintin 2009). Chemical destabilization of microencapsulated n-3 ingredients in food matrices causing unacceptable off-flavor has planted a seed of uncertainty and distrust in the consumer's mind.

CONCLUDING REMARKS

Current knowledge relating to oxidation mechanisms and microencapsulation techniques has allowed the design of functional foods enriched with n-3 LCPUFAs. Strategies involving the use of novel microencapsulation techniques along with the use of a combination of antioxidants and improved packing have helped increase the stability of such products. However, product development has been limited to short to medium shelf-life products because of oxidative deterioration and lack of stability during long-term storage. However, it must be emphasized that the n-3 LCPUFA-enriched foods should be stable and convenient, have acceptable taste/flavor, and be without heavy price premiums in order to have an effective population-wide increase in consumption of these bioactive fatty acids.

There is no doubt that the inclusion of n-3 LCPUFAs into food products can be achieved, but novel approaches may be required to achieve the target outcomes. A multidisciplinary effort between food manufacturers, food technologists, food scientists, and packaging technologists may be required. With the ongoing developments, the n-3 LCPUFA market is certain to grow in the future, which is good news for consumers, who are bound to reap the health benefits.

This raises the question of whether fish oil producers will be able to meet the imminent demand (Surette 2008). It has been recently reported that 90% of the bigger fish species, such as the blue fin tuna (high in n-3 LCPUFAs), have been fished out and are on a path to extinction. Meanwhile, millions of people are joining the middle class in developing countries, leading to an increase in the consumption of seafood globally from 10 kg per person per year in the 1960s to 17 kg per person per year at present (Walsh 2011). However, the worldwide fishing catch has been steady at 80 million tons per year since the mid-1990s. Farmed fish through aquaculture have been filling the gap between world seafood consumption and worldwide fish catch with 47.5 million tons production in 2008. Fish farmers have been constantly involved in fish breeding to meet the growing demand. Fish biotechnologists have taken it one step further by planting a gene from Chinook salmon into Atlantic salmon that increased the overall growth up to two times as fast as conventional fish (Walsh 2011).

Development of transgenic varieties of common plants, such as canola, soybean, and safflower, with high levels of stearidonic acid, EPA, and DHA are also being researched as alternatives to fish oil. Novel plants that are abundant in stearidonic acid, such as *Echium plantagineum* (commonly known as Paterson's curse) are also being grown. Stearidonic acid is metabolized into EPA and DHA much more efficiently by our body than ALA (Surette 2008). Genetically modified fish and plant species might help solve the food security issue in the future; however, current food and environmental safety regulations might need amendments for faster transition from development to market (Potrykus 2010).

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