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The New Paradigm for Lipid Oxidation and Insights to Microencapsulation of Omega-3 Fatty Acids

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Abstract: The consumption of omega-3 fatty acids provides a wide range of health benefits. However, the incorporation of these fatty acids in foods is limited because of their high oxidative instability. A new paradigm has emerged to better explain the oxidation mechanism of polyunsaturated fatty acids, which will be discussed here with reference to bulk lipids considered a special case of water in oil microemulsion. This paradigm suggests that lipid oxidation reactions are initiated by heterogeneous catalysis by metal oxides followed by the formation of micelles containing initial hydroperoxides, water, and other amphiphilic compounds. The induction period comes to the end when the formed micelles reach a critical micelle concentration and start to decompose opening the way to intense free radical reactions. Antioxidants and synergists extend the induction period not only by scavenging free radicals but also by stabilizing the micelles. With better understanding of the lipid oxidation mechanism, a tailored choice of antioxidants and synergistic combinations, and efficient encapsulation methods may be optimized to provide stable encapsulates containing highly n-3 polyunsaturated fatty acids. Smart processing and encapsulation technologies utilizing properly stabilized oils as well as optimized packaging parameters aiming to enhance n-3 fatty acid stability by smart selection/design of antioxidants, control of the interfacial physics and chemistry, and elimination of surface oil are needed for this purpose.

Keywords: encapsulation, free radical chemistry, heterogeneous catalysis, lipid oxidation, omega-3 fatty acids

General Introduction to the Challenges Facing the Incorporation of Omega-3 Polyunsaturated Fatty Acids in Foods

Omega-3 polyunsaturated fatty acids (n-3 PUFA), especially eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), have been shown to provide several health benefits to humans, for example against rheumatism, inflammation, psychiatric and neurodegenerative illnesses, dyslexia, depression, schizophrenia, autism, type 2 diabetes, coronary heart disease, atherosclerosis, cancer, and Alzheimer's disease (Calder 2013). However, the incorporation of n-3 PUFA isolated from fish tissues into foods is challenged by their extreme instability toward oxidation, which is caused by the high number of double bonds in their chemical structures. The inhibition of lipid oxidation reactions, especially for highly unsaturated fatty acids such as EPA and DHA, has been a challenge throughout the past century. Efforts made during the past decades to use primary antioxidants (mainly tocopherols) together with certain synergists to stabilize n-3 PUFA for utilization in foods were not very successful.

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Jacobsen (2015) reviewed the strategies used for the stabilization of foods enriched in n-3 PUFA and addressed the importance of optimization of antioxidant addition and processing parameters. It was suggested that the use of multiple antioxidants with multifunction properties (radical scavenging, metal chelating, oxygen scavenging, singlet oxygen quenching, and antioxidant regeneration) may provide better protection than monocompound antioxidants. However, despite a general agreement about these strategies, a convincing understanding of the antioxidant cooperation mechanism(s), known as synergism, is not yet attained. To reach a practical solution to the lipid oxidation challenge, a better understanding of the chemistry and physics of the reactions involved, especially at the initial stages of the transformations, is required.

Besides antioxidant addition, encapsulation was employed as a secondary approach to further protect n-3 PUFA against oxidation and to facilitate their incorporation in food products such as bread, yoghurt, milk, and infant formulae (Barrow and others 2013). Encapsulation, referring to the embedding of the oil in a matrix of proteins and/or carbohydrates, can be achieved through a variety of processing techniques including for instance spray granulation, spray drying, and freeze drying. The stability of the encapsulated n-3 PUFA depends on several parameters including oil quality, stabilizing antioxidants and synergists, oil distribution within the particle, particle size and surface area, particle density, wall material, moisture content, and water activity. A major challenge facing encapsulation processes is related to the small percentage of

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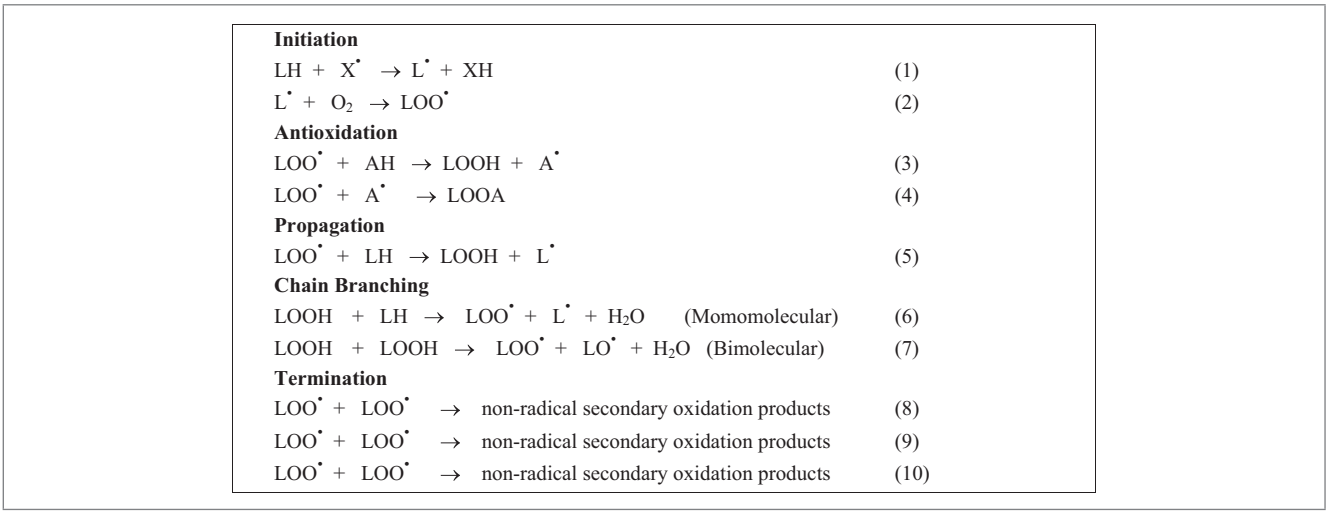

Figure 1–Schematic description of the accepted mechanism of the important free radical reactions during the initiation, propagation, and termination of lipid oxidation chain reactions.

surface oil spread as a thin layer over the surface of the capsule, which makes it quite vulnerable to oxidation (Velasco and others 2006; Ruiz-Ruiz and others 2017). If processing conditions and ingredients are selected appropriately, it would be possible to prepare highly stable n-3 PUFA encapsulates.

It is well known that lipid oxidation reactions start by the transformation of lipids, especially those containing unsaturated double bonds, to lipid hydroperoxides via the free radical mechanism. These hydroperoxides degrade to a wide variety of secondary oxidation products (including alcohols, aldehydes, ketones, epoxides, dimers, and polymers) leading to organoleptic changes and rancidity (Schaich 2012). It became apparent in the last 2 decades that interfacial phenomena, to be discussed in detail later, play an important role in lipid oxidation reactions, which led to this change of paradigm. Thus, understanding of the physical chemistry of the oxidation reactions is necessary with particular reference to heterogeneous catalysis by metal oxides (Cheng and Li 2007) and the role played by micelles (Brimberg 1993). The combination of free radical chemistry with heterogeneous catalysis by trace metal ions and micelles provides satisfactory explanation for many of the phenomena that cannot be explained on the mere basis of the free radical mechanism (Budilarto and Kamal-Eldin 2015a). The involvement of the interfacial layer in lipid oxidation in emulsions and multiphase systems has been reviewed (Berton-Carabin and others 2014).

In this article, we review the new concepts focusing on the multidimensional characteristics of lipid oxidation and the important role of hydrophilic–lipophilic properties of the different molecular species present in an oxidizing system. Although this paradigm will apply to the general case of lipid oxidation (in bulk lipids, water-in-oil emulsions, and oil-in-water emulsions), this review will focus on oxidation in bulk lipids as a special case of water-in-oil microemulsion (Chaiyasit and others 2007, 2008; Chen and others 2010, 2011a, 2011b). We shortly present lipid oxidation reactions as explained by the free radical mechanisms and then link the roles played by heterogeneous catalysis with the chemical reactions occurring during the initiation, propagation, and termination steps of the lipid oxidation reactions. After laying these foundations, we review knowledge pertinent to how lipid oxidation is affected by the degree of unsaturation, humidity, antioxidants, and synergists and antagonists. Finally, we discuss how this new knowledge may provide opportunities for tailored choice of antioxidant and synergistic combinations and preparation methods to provide stable nano- and microencapsulates containing n-3 PUFA. The understanding of this extended model is vital for food engineers and processing technologists interested in preparation of stable n-3 PUFA ingredient formulations.

Lipid Oxidation as Explained by the Free Radical Mechanism

The current knowledge about the lipid oxidation mechanism is gathered by analysis of oxidation products and kinetic studies. During the 1940s, lipid hydroperoxides (LOOH) were identified as the primary lipid oxidation products (Farmer and Sundralingam 1942; Farmer and Sutton 1943, 1946) and the free radical mechanism of lipid oxidation was proposed (Bolland 1946, 1950; Bolland and Gee 1946a, 1946b). It is largely accepted that lipid oxidation reactions are explained by the classical free radical chain mechanism presented in Figure 1. The sequence of reactions is accepted to include 3 stages identified as initiation, propagation, and termination periods.

(i) The initiation phase (or induction period IP) comprising the monomolecular phase of hydroperoxide formation and peroxyl radical scavenging by antioxidants,
(ii) The propagation phase (or exponential stage) including the autocatalytic and the monomolecular and bimolecular or branching reactions, and
(iii) The termination stage mainly characterized by hydroperoxide decomposition and increased formation of secondary oxidation products.

Kinetically, the lipid oxidation reactions show the features of chain reactions autocatalyzed by its products, the peroxyl radicals as shown in Figure 1. The chemistry explaining the different products observed during lipid oxidation reactions is elegantly presented by Schaich (2012). During the cascade of the reaction, lipid hydroperoxides degrade to secondary oxidation products including lipid alcohols, ketones, epoxides, oligomers, and β-scission released volatiles. The formation of these compounds is minimal during the initiation phase but increases exponentially during the propagation and termination phases. When phenolic antioxidants are present, they act as hydrogen donors (AH) and scavenge

chain-propagating peroxyl radicals and, thereby inhibit the oxidation reactions (Porter 1993; Kamal-Eldin and Appelqvist 1996).

Although the very initial stage(s) of lipid oxidation are the most important when it comes to impact and consequences, scientific investigations have mainly focused on the propagation and chain branching reactions describing the exponential increase in the concentration of hydroperoxides after the initial period of slow reaction known as the induction period (IP). It is important to note here that this approach often gave paradoxical results and inconsistencies. The main paradoxical features that are not explained by the free radical mechanism are those related to critical phenomena manifested in the oxidation of fatty acid substrates and its inhibition by antioxidants (Kamal-Eldin and Budilarto 2015a) such as;

(i) The criticality governing the sudden change from the initial reaction phase (induction period) to the exponential propagation phase. This sudden change in reaction rates of the same chemical reactions can only be explained by a critical change in the reaction microenvironment, the organization of molecular species, and proximity of interacting species (Laguerre and others 2017),
(ii) The loss of antioxidant efficacy with increased antioxidant concentrations. With α-tocopherol taken as a typical example, the rate of oxidation during the IP increases with increased antioxidant concentration (see explanation in Section "Antioxidants"). and
(iii) The unexplained synergistic interactions between primary antioxidants (phenolic type) and secondary antioxidants (examples phospholipids and amino acids).

Thus, the free radical mechanism alone does not unequivocally provide a detailed and circumstantial description of the physical and chemical changes of reactants to products, including the characterization of the composition, structure, energy, and other properties of reaction intermediates, products, and transition state(s). Gradually, a change in paradigm occurred in relation to these criticalities. Several breakthroughs have led to this change starting with the publication of Porter's (1993) treatise on the antioxidant paradox, Frankel and others (1994) suggestion of the interfacial phenomenon, and its refining by Decker's group to include association colloids (Chaiyasit and others 2007, 2008; Chen and others 2011a, 2011b); the cut-off theory (Laguerre and others 2009, 2015), and the involvement of micelles (Brimberg and Kamal-Eldin 2003; Budilarto and Kamal-Eldin 2015a, 2015b).

Heterogeneous Catalysis and Lipid Oxidation in Bulk Oils

Previously, lipid oxidation reactions in bulk oils were considered to occur in homogeneous solutions by the free radical mechanism. Currently, it is well accepted that bulk oils have colloidal structures based on reversed micelles and/or lamellar dispersions known as association colloids (Chaiyasit and others 2007, 2008; Chen and others 2010; Xenakis and others 2010). This type of structure supports heterogeneous rather than homogeneous catalysis. Heterogeneous catalysts have multiple types of active sites, which qualifies dispersible colloids and nanoclusters as heterogeneous catalysts (Astruc and others 2005). In the new understanding, the colloidal structure and the different catalytic surfaces play an important role and may explain many of the paradoxes associated with mechanisms solely based on the free radical mechanism.

The very initial phase of lipid oxidation

In literature, the initiation phase of lipid oxidation is generally represented by the general equation (1) where neither the type of the hydrogen acceptor $X^{\bullet}$ nor of the nature of the reaction(s) is precisely described. Actually, Privett and Plank (1962) published an important investigation on the initial stages of autoxidation and concluded that "the oxidation of polyunsaturated lipids is initiated by a discrete reaction occurring prior to the formation of stable hydroperoxides." These authors recognized that the reaction(s) involved are very slow and irreproducible, which is in agreement with the nature of heterogeneously-catalyzed reactions (Mikhailov 1999). Irregular shapes of oxidation curves during the very early stage of lipid oxidation were obtained by different authors (Spranger and others 1998). However, the importance and contribution of this very initial phase to the autocatalytic lipid oxidation reaction driven by peroxyl radicals is seldom discussed. Nevertheless, it seems to be the most important and most difficult to control.

It is well agreed that lipid oxidation is initiated by interactions of PUFA with energy (temperature or light) in the presence of catalytic amounts of transition metals leading to the abstraction of a hydrogen atom from PUFA and the generation of first free radicals. This oxidative dehydrogenation, by heterogeneous catalysis, provides a convincing explanation to the initiation of lipid oxidation. It is well known that transition metal ions catalyze the initiation of lipid oxidation and that the rate of initiation is proportional to the concentration of trace metal ions (for example, cobalt, copper, iron) in their low or high transition states (Schaich 1992). Since the C–H bonds of hydrocarbons are very weakly acidic, the surface sites capable of the deprotonation of hydrocarbons must be basic (Burch and others 1999) and metal oxides can provide such catalysts in the nanoscale. The following equations explain the mechanism of catalysis by metal oxides,

$$LH + M^{(n+1)+}\text{-}OH \rightarrow L^{\bullet} + M^{n+}\text{-}OH_2 \quad (1)$$

$$LOOH + M^{n+}\text{-}OH_2 \rightarrow LO^{\bullet} + M^{(n+1)+}\text{-}OH + H_2O \quad (2)$$

According to this mechanism, metal oxides are able to form hydrogen bonds with the labile hydrogens of unsaturated fatty acids in a similar way to lipoxygenase and cyclooxygenase enzymes and initiate oxidation by hydrogen abstraction (Schneider and others 2007). The only difference between the enzymatic and nonenzymatic metal-catalyzed oxidation pertains to the regio- and stereospecificity of the enzymes, which are determined by the space and the structural features of the proteins at their active sites (Liavonchanka and Feussner 2006). In the catalytic oxidation of an olefin, $R_1–CH = CH–CH_2–R_2$ by transition metal oxides, the olefin is adsorbed on the surface of the metal and a hydrogen atom is absorbed leaving a $R_1–CH = CH–CH^{\bullet}–R_2$, which will react with oxygen to produce the initial hydroperoxides. The mechanism of "oxidation by dehydrogenation" may explain some observations that are not yet understood. For example, that compounds with *trans* double bonds oxidize at lower rate than compounds with *cis* double bonds and that oxidation of saturated lipids is also possible at high temperature (Brodnitz 1968). Depending on the degree of refining, vegetable oils may contain up to 800 ppb of iron and copper (Llorent-Martinez and others 2011).

The role of transition metal contaminants and catalytic surfaces may be described to resemble in essence the role of oxygenases,

particularly lipoxygenases. It is agreed that the first step in the enzymatic catalysis of lipid oxidation is the activation of the fatty acid substrates by iron in the active site of the enzyme and that the Fe(III) to Fe(II) redox state is absolutely essential for enzyme activity. It was shown that in reactions initiated with Fe(II) lipoxygenase that there is a kinetic lag phase or "induction period", which is inversely proportional to the lipoxygenase concentration (Veldink 1994). The initial reaction produces hydroperoxides, which reduce the ferric to ferrous and reactivate the enzymatic catalysis. This initial reaction is highly nonlinear but it will eventually approach a steady state where the oxygen consumption becomes a linear function of time (Schilstra and others 1993; Wang and others 1993; Glickman and Klinman 1995). The active sites of lipoxygenases were shown to be inhibited by secondary oxidation products and corresponding alcohols (Waller and others 2008). On the other hand, phenolic antioxidants, such as α-tocopherol, seem not able to inhibit reactions in the lipoxygenase catalytic pocket but can inhibit the subsequent free radical reactions catalyzed by hydroperoxides (Noguchi and others 2005). In other metal oxide-catalyzed oxidations, it is possible that phenolic antioxidants present some competitive inhibition to the dehydrogenation of unsaturated fatty acids but this will depend on their structures and concentrations.

In another complication, iron and other transition metal ions can catalyze the production of highly reactive oxygen species through Haber Weiss reaction (Gülçin 2006):

$$O_2^{\bullet -} + H_2O_2 \rightarrow O_2 + OH^- + OH^{\bullet} \quad (3)$$

Where in the presence of Fe^{2+} or Cu^{2+}, H_2O_2 can form $OH^{\bullet}$ by the Fenton reaction (Gülçin 2006). Many antioxidants are known to form chelates with Fe^{2+}, which is the most powerful pro-oxidant among the various species of metal ions. Flavonoids, for instance, are not only known for their scavenging of radical activities (Silva and others 2002) but also for their metal chelating activities (Hall 2001). The flavonoids binding sites for metals are also related to the phenolic groups responsible for radical scavenging (Amić and others 2007). All of these intervening aspects deserve new investigations that will push forward the understanding of induction period and the role of metal chelating activities of antioxidants.

The induction period (the steady state oxidation)

After the initial heterogeneous catalysis of oxidation by dehydrogenation reactions, a period of slow steady state formation of hydroperoxides commences and the initial hydroperoxides formed will start to disperse in the continuous phase of lipids. In the absence of inhibitors, the rate of oxidation during this period, commonly known as the induction period (IP) shows a linear (zero order or pseudo-first order) dependence on the concentration of unsaturated lipids and hydroperoxides (Sullivan and others 2011). It was shown that during the induction period, the initiation reactions are dominated by monomolecular decomposition of hydroperoxides (Bateman and others 1953),

$$LOOH \rightarrow LO^{\bullet} + OH^{\bullet} \quad (4)$$

However, this reaction may be facilitated by a reducing agent (X-H), such as a highly reactive PUFA

$$\begin{array}{l} LO\text{-}OH \rightarrow LO^{\bullet} + X^{\bullet} + H\text{-}OH \\ \quad\vdots \\ X\text{-}H\ (\text{Reducing agent}) \end{array} \quad (5)$$

It is also well known that the rate of lipid oxidation in bulk oils increases when hydroperoxides are generated or added to a substrate (Kern and Willersinn 1955). Lipid hydroperoxides are amphiphilic molecules with the dual characteristics of lipophilic and lipophobic domains, that is lipophilic hydrocarbon tail and hydrophilic –OOH groups. Amphiphilic hydroperoxides act as surface-active molecules and reorganize themselves to form reversed micelles in bulk lipids (Moulik 1996; Dalby and Care 1999). According to Brimberg and Kamal-Eldin (2003), oxidation enters the exponential stage when the hydroperoxides reach their critical micelle concentration (CMC) in lipid substrates. When the concentration of hydrperoxides and other amphiphiles in lipids exceeds a certain CMC, they start to form micelles. With increased formation of micelles (containing hydroperoxides, other amphiphiles, and water formed by reactions 8 and 10), an interfacial environment is established in a previously neat oil-phase. These interfaces will be the sites of oxidation/antioxidation reactions. The changes in properties that occur as micelles form are marked by sharp transitions in many physical quantities such as the surface tension, viscosity, conductivity, and turbidity of the solution (Stupp and others 1997; Ramanathan and others 2013; Lombrado and others 2015). These changes coincide with the end of the induction period at least in frying oils (Choe and Min 2007).

The exponential phase (or the bimolecular phase of hydroperoxide formation and decomposition)

The polar groups in the interior of the reversed micelles containing lipid hydroperoxides, co-existing amphiphiles, and water molecules are disordered in a small volume. As the concentration of amphiphilic compounds increases, the micelles grow in number and size until their concentration is large enough that they aggregate and interact to form mesophases (Brimberg and Kamal-Eldin 2003). Coagulation is then followed by flocculation of lipid hydroperoxides and other amphiphiles leading to the formation of fragile clusters followed by coagulated networks of distinct structural ordering and macroscopic properties. Variations in the structure of lipid hydroperoxide affect their entrapment and localization in the flocculates, the distances between them, their mobility, rates of diffusion, and collisions leading to the bimolecular decomposition facilitating the exponential oxidation stage. When hydroperoxide molecules are close enough, they form bimolecular associations and then decompose into free radicals (Bateman and others 1953; Paízková and others 1989).

$$\begin{array}{l} 2\ ROOH \rightarrow R\text{-}O\text{-}O\cdots\cdots H\text{-}O\text{-}O\text{-}R \rightarrow RO^{\bullet} + ROO^{\bullet} + H_2O \\ \qquad\quad | \\ \qquad\quad H \end{array} \quad (6)$$

The transition from monomolecular decomposition (reaction 6) to bimolecular decomposition (reaction 7) was mentioned to occur at lipid hydroperoxide concentration of approximately 0.2 M and the rate constant of the bimolecular decomposition of linoleate hydroperoxides at 55 °C was calculated as 50×10^{-6} $M^{-1}s^{-1}$ (Bateman and others 1953).

Manifestation of self-organization processes in the chemistry of materials is documented and can reasonably explain the nonlinear chemical transformations and associated critical states (Tretyakov 2003). Figure 2 shows how molecular hydroperoxides are arranged into micelles during the course of lipid oxidation. The phase transitions induced by the hydroperoxides are modulated by 2 types of surfactant agents affecting the interfacial tension and interfacial

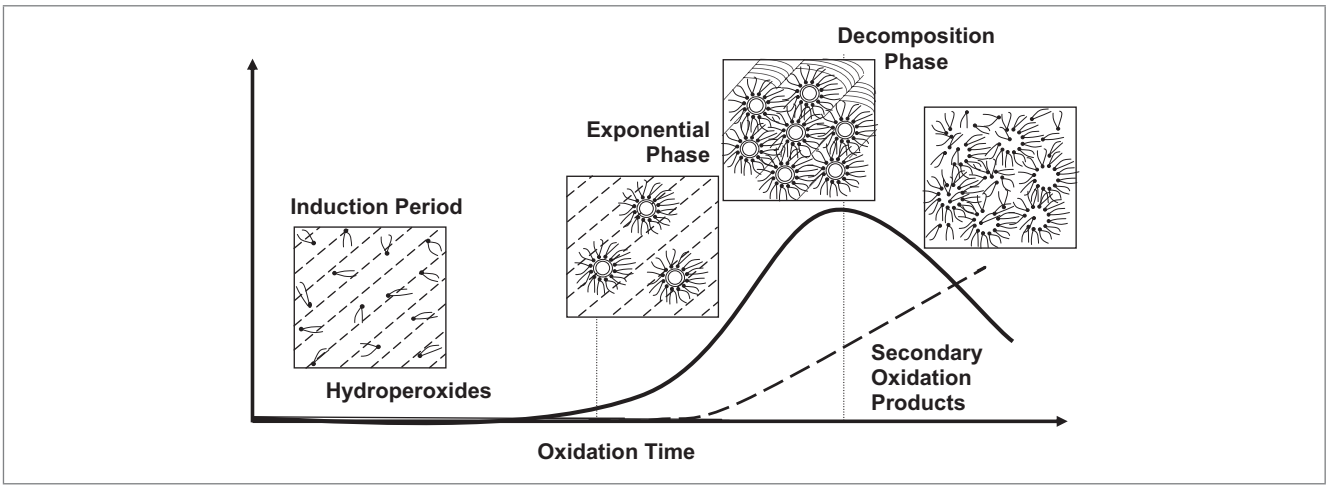

Figure 2–Schematic representation of the evolution of hydroperoxides and secondary oxidation products during lipid oxidation (heterogeneous catalysis by micelles). When the concentration of hydroperoxides produced by catalysis by metal oxides is stable, the oxidation enters the steady state (or the induction period), during which the reaction is catalyzed by monomolecular decomposition of the hydroperoxides ($LOOH + LH \rightarrow LO^{\cdot} + L^{\cdot} + H_2O$). As the concentration of hydroperoxides increases, phase transformations can explain the criticality associated with the transition from the induction period to the exponential stage, where the bimolecular decomposition of the hydroperoxides is the dominant mechanism ($LOOH + LOOH \rightarrow LO^{\cdot} + LOO^{\cdot} + H_2O$). The contribution of the different indigenous amphiphilic compounds and oxidation products to the different phase transitions are appreciated but largely unknown.

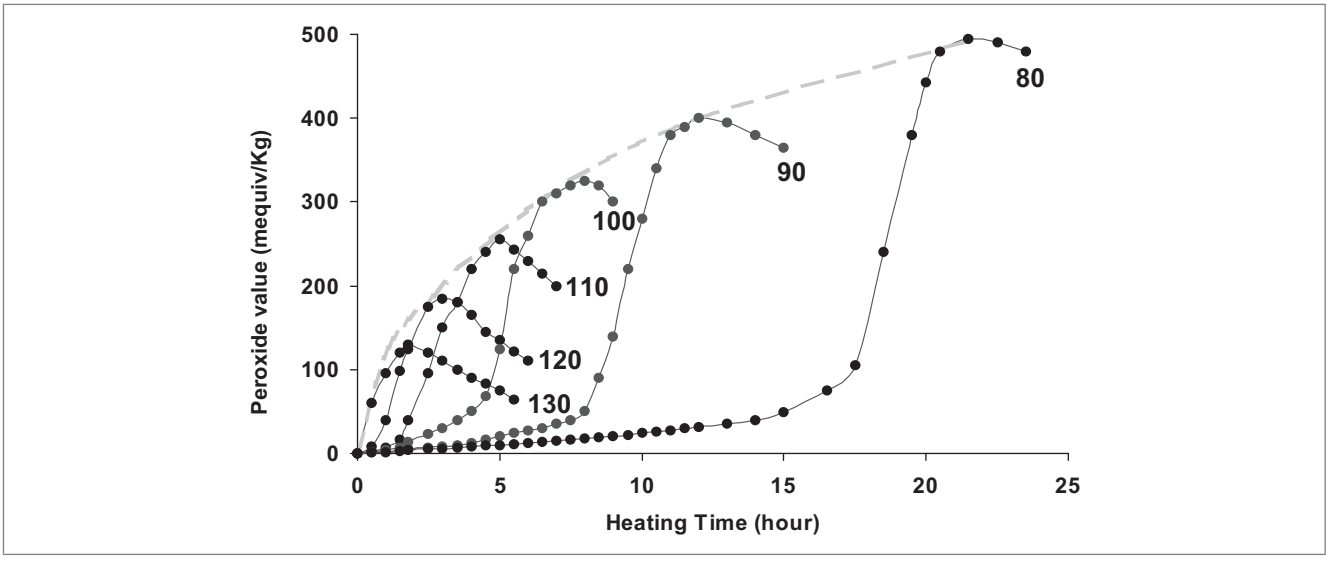

Figure 3–Temperature is the most significant factor affecting lipid oxidation rates. This figure shows the formation of hydroperoxides during the oxidation of linseed oil at 80 to 130 °C (Data from Hess and O'Hare 1950). The effect of temperature is a complex including increasing the rate of hydroperoxides formation and their decomposition by affecting chemical reactivity as well as the organization and stability of colloidal structures. The effect of temperature on lipid oxidation needs to be redefined with the new understanding reviewed in this paper.

free energy of the reaction mixture. Emulsifiers, such as phospholipids, reduce the interfacial tension and interfacial free energy and inhibit the flocculation keeping the hydroperoxides apart and lowering their reaction rates. On the other hand, molecules such as sterols and alcoholic hydrocarbons may function as surfactants and enhance the rate of flocculation as will be discussed later. Reactions are not only driven by the chemical potential gradient (namely, substrate, oxygen partial pressure, catalytic agents including hydroperoxides, antioxidants) but also by the temperature and pressure gradients. The reaction rate is determined by the sum of effect of these driving forces but these forces work in different directions. For example, while increased production of hydroperoxides tends to make the system less spatially homogeneous, temperature increases diffusion and brings in more spatial homogeneity besides its effect in increasing the monomolecular decomposition of hydroperoxides (Figure 3). In addition, temperature has its own effects on phase equilibria and destabilization of micelles, an effect that seems to be nonlinear. Nonlinearity is, thus, a natural consequence of the chemical and physical transformations in the system and their interactions. In the future, the effect of temperature on colloidal structures and its contribution to lipid oxidation rates needs to be further specified.

Chain termination

Chain termination reactions take place when the fatty acid substrates start to diminish. In this case, peroxyl and alkyl radicals

undergo radical–radical combinations according to reactions 4 to 6. The temperature of the reaction and availability of oxygen will determine the type of adducts formed LOO-OOL, LOOL, and L-L. The tetroxide LOO-OOL decomposes in the solvent cage by the Russel (1957) mechanism into alcohol, ketone, and singlet oxygen

$$L_1OOOOL_2 \rightarrow L_1{=}O\cdots + L_2OH + {}^1O_2 \qquad (7)$$

The formation of lipid hydroperoxides and their decomposition to secondary oxidation products in proportion to the lipid substrates is minimal during the induction period but increases significantly afterwards. When the lipid substrates are about to diminish and the concentration of hydroperoxides reaches another critical point with regard to the self-organized character of the system, hydroperoxides start to exponentially decompose to secondary oxidation products including aldehydes, ketones, dimers, oligomers, and so on (Chan 1987). Despite the large diversity of secondary oxidation products that have been isolated and characterized, the entire product profiles and the kinetic factors affecting their formation and relative abundance are largely unknown. In agreement with this, there is no knowledge about the contribution of the different secondary oxidation products to the overall colloidal structure, phase equilibria, and phase transformations. However, although the secondary oxidation products are more polar than the hydroperoxides and are expected to contribute to greater changes in the physical structure of the reaction mixture, these changes are of less practical importance since earlier changes in organoleptic properties are more significant with reference to the acceptance of the lipids.

In conclusion, the consideration of the bulk lipids as colloidal dispersions and the role of association colloids (reversed micelles and lamellar structures) as nano-reactors that influence the kinetics and mechanism of lipid oxidation reaction seem to offer new horizons for a better understanding of lipid oxidation and the protection of food lipids, particularly the more sensitive n-3 fatty acids.

The Participation of Different Molecular Species in the Oxidation of Bulk Lipids

Dietary lipids are mostly dominated by fatty acids in the form of triacylglycerols but contain variable mixtures of different lipophilic and amphiphilic compounds that, although minor, structure the lipids into bulk oil or emulsion. According to the new paradigm (Chaiyasit and others 2007, 2008; Chen and others 2011a, 2011b, 2012; Budilarto and Kamal-Eldin 2015a, 2015b), various compounds play significant role(s) in the stability of dietary lipids. Therefore, it is important to discuss the individual contributions of the different molecular species to lipid stability.

Unsaturated fatty acids

A wide range of studies have been performed on the oxidation of bulk lipids as vegetable oils and their purified triacylglycerols, or as model fatty acid methyl esters, in the presence and absence of different additives. When some level of antioxidative tocopherols is present, the stability of vegetable oils is very much influenced by their fatty acid composition (Kamal-Eldin 2006). It is well known that the rate of lipid oxidation increases with increased number of double bonds; the relative rates of oxidation of oleic, linoleic, and linolenic acids in neat oils were reported as 1:40 to 50:100, respectively (Holman and Elmer 1947). *Hitherto*, the discussion of the influence of double bonds on fatty acids' stability has focused on the number of "sensitive" hydrogens and the ease of their abstraction by hydroperoxyl radicals. However, there is an additional effect of the presence of double bonds in the fatty acids and their triacylglycerols as it also affects their 3-dimensional structure and coagulation behavior. The presence of double bonds in the triacylglycerol molecules causes curvature and adds some surface activity compared to triacylglycerols having saturated or monounsaturated fatty acids. In fact, there is some literature supporting the importance of fatty acids conformations on their oxidative stability. For example, elaidic acid (18:1n-9*trans*), which is similar to stearic acid in molecular formula, is significantly more stable than its *cis* isomer oleic acid (Feuell and Skellon 1952). In this and other studies, the oxidative stability was also found to increase in the order oleic acid < methyloleate < ethyloleate < n-propyloleate < n-butyloleate. In the case of triacylglycerols, the position of the fatty acid molecules in the triacylglycerols affects their rate of oxidation. For example LnLnL was found slightly more stable than LLnLn and LLLn was more stable than LLnL pointing to some increased stability of the fatty acids at sn-2 position of the triacylglycerols (Miyashita and others 1990, Neff and El-Agaimy 1996). Similarly, triacylglycerols containing DHA show higher oxidative stability when this fatty acid exists at the *sn*-2 position rather than at the *sn*-1(3) position (Wijesundera and others 2008). These differences may be attributed to the variation in physical orientation of the fatty acids in different positions and the interaction with the head groups of the peroxyl radicals. The effect of the 3-dimensional conformational structure of EPA and DHA on their oxidizability is not yet clear. According to Miyashita (2014), the PUFA conformation at the interface is a very important determinant of their oxidative stability that is affected by the PUFA structure and the interactions between the PUFA and the other molecules. One question that needs to be answered through future research is "*Should highly unsaturated fatty acid ingredients be prepared as liquid triacylglycerols, emulsions, or soapy fatty acid salts*?". Preparation of fatty acid salts may enable better incorporation and mixing of stabilizing agents including suitable synergists that control of the water activity and aid emulsification of these preparations (Baik and others 2004; Champagne and Fustier 2007).

Hydroperoxides

The accumulation of hydroperoxides during the induction period leads to a hydrophobic mismatch with the triacylglycerols especially when the concentration of hydroperoxides reaches a CMC. The CMC for the methyl linoleate hydroperoxides in methyl linoleate of about 10–20 mM, corresponds to the critical concentration of hydroperoxides at the inflection point between the induction period and the exponential phase of lipid oxidation. Hydroperoxides may behave as surfactants and stimulate the formation of reversed micelles depending on their hydrophilic-lipophilic balance (HLB) and on the other chemical and physical conditions of the system. Kern and Willersinn (1955) studied the initiating effect of different peroxides on the oxidation of methyl linoleate. The catalytic effect of hydroperoxides increased parallel with their lipophobicity, that is with the increased ease of reverse micelle formation. When the rate of oxidation catalyzed by different hydroperoxides was plotted versus oxidation level, all lines were parallel indicating no change in mechanism despite the differences in the catalytic activity of different hydroperoxides. Ethyl esters of EPA and DHA oxidized rapidly at 5 °C in the dark after an induction period of 3–4 days, compared to linolenate and linoleate esters with induction periods of 20 and more than 60 days, respectively (Cho and others 1987). The hydroperoxides of EPA and DHA are

more polar and less stable than those of linoleic and linolenic acids (Yazu and others 1998). The effect of the hydrophilic-lipophilic balance of the resulting hydroperoxides (and other oxidation products) is yet another factor that complicates the determinants of the lipid oxidation outcomes.

Recently, Laguerre and others (2017) discussed the role of mass transport phenomena in lipid oxidation and antioxidation. They identified 3 different mechanisms for the movement of lipid hydroperoxides from 1 particle to another; (a) diffusion, (b) collision-exchange-separation, and (c) micelle-assisted transfer. These authors explained that when lipid hydroperoxides reach their CMC, they shift their mass transport from the slow collision-exchange-separation pathway to fast micelle-assisted transport mechanism. With the same phenomena applying to antioxidants and other surface-active compounds in oxidizing lipids, this emphasizes the importance and complexity of the involvement of micelles in lipid oxidation pathways.

Water

Depending on their degree of refining and the level of minor lipid components, vegetable oils contain variable amounts of water, which can be up to 1% (Chen and others 2011b). In addition, water is also formed during the course of lipid oxidation as a result of reduction of hydroperoxides (Budilarto and Kamal-Eldin 2015a). The presence of water was found to exert prooxidant activity during lipid oxidation in foods at low and high water activities and an antioxidant effect at intermediate activities (Labuza and Dugan 1971). Water activity was reported to have a considerable influence on the length of the induction period in the oxidation of methyl linoleate at 37 °C. At low water activity (aw = 0.22), the presence of water has stimulated oxidation. As the water activity increases, aw = 0.32, it starts to form hydrogen bonds that solubilize, dilute and stabilize hydroperoxides with maximum stabilization at aw = 0.67 (Gopala-Krishna and Prabhakar 1992). At low levels, water may act as an antioxidant by hydrating or diluting catalytic metal oxides (Chen and others 1992) but as its content increases, it may act as a prooxidant by the solubilization of these catalysts (Labuza and others 1971). After the induction period, water activity has no effect on the rate of oxidation but has an effect on the profile of secondary oxidation products (Gopala-Krishna and Prabhakar 1992). In fact, the addition of 0.25-1.00% water tremendously improved the stability of crude peanut oil but not of degummed oil (Gopala-Krishna and Prabhakar 1995). The effect of water binding agents on the rate of lipid oxidation depends on the water activity but in the presence of glycerol, the prooxidant effect of water was found to predominate at all water activities (Heidelbaugh and Karel 1970). The presence of electrolytes increases the interfacial tension due to salting out of the emulsifiers leading to decreased emulsion stability (Komaiko and others 2016).

Antioxidants

The effect of antioxidants on lipid oxidation has been paradoxical with respect to antioxidant structure and concentration (Porter 1993; Kamal-Eldin and Appelqvist 1996). It is already well established that there is an optimum concentration of a given antioxidant for maximum stability of a given substrate, above which the antioxidant may experience a *loss of efficacy*. This loss of efficacy was attributed to the participation of the antioxidant itself or its radical(s) in peroxidatiove side reactions. It was suggested that α-tocopherol loses antioxidant efficacy because of the participation of its molecule in 1 peroxidative reaction as well as the participation of its radical in more than 1 pro-oxidative reactions (Yanishlieva and Marinova 1992). The main reactions responsible for the peroxidative effect of α-tocopherol were shown to include chain transfer reaction at the abstraction of hydrogen atom from the fatty acid molecule and from the hydroperoxide by tocopheroxyl radical, an initiation reaction involving a reducing effect of α-tocopherol on hydroperoxides, and reactions of homolytic decomposition of quinolide peroxides (Tavadyan and others 2007). However, because of the surfactants and anti-coagulation effect of α-tocopherol (log P = 9.04), the CMC is higher in samples containing tocopherols compared to controls or samples containing low concentrations of the antioxidant (Brimberg and Kamal-Eldin 2003). Thus, the presence of high concentrations of α-tocopherol contributes to decreasing the interfacial tension and stabilizing the micelles, which explains why it prolongs the induction period despite the increase of the rate of oxidation during the induction period. In accordance with the polar paradox, α-tocopherol analogues with shorter phytyl tails (6 or 11 carbons) showed greater antioxidant activity in biomembranes compared with α-tocopherol with 16 carbons in the tail (Kagan and others 1990). Similarly, less lipophilic γ-tocopherol (*log P* = 8.98) and δ-tocopherol (*log P* = 8.60) are better antioxidants than α-tocopherol in bulk oils (Huang and others 1994, Yanishlieva and others 2002) possibly due to greater stabilization of the micelles during the induction period. So far studies comparing the antioxidant behavior of the tocopherol homologues have focused on their chemical reactivities but more emphasis on their emulsification properties is required in future studies. The 2 effects, that is radical scavenging and micelle stabilization, are correlated since they are influenced by the number of *ortho* methyl substituents in the phenolic rings (2 in α-tocopherol, 1 in γ-tocopherol, and none in δ-tocopherol).

In this review, bulk lipids are considered a special case of water-in-oil microemulsions in which lipid hydroperoxides and other amphiphilic compounds concentrate in the interface between the continuous oil phase and the small amounts of water. Studies with esters of antioxidant phenolic acid esters having different alkyl chain lengths presented a challenge to the polar paradox theory (Torres de Pinedo and others 2007). The optimum chain length for maximum antioxidant effects of esters of chlorogenic acid, dihydrocaffeic acid, hydroxytyrosol, rosmarinic acid and rutin in model emulsions was found in the range of C8-C12. This nonlinear, ʌ-shape, relationship found between antioxidant polarity and effectiveness in emulsions is referred to as the cut-off effect (Laguerre and others 2009, 2017). The relation between antioxidant polarity and potency is not always linear since the actions of antioxidants is determined in a complex manner by their hydrogen-donation ability, molecular partitioning, hydrogen bonding, interphase transport, surface accessibility, micelization, and interactions with lipids, hydroperoxides, trace metals, emulsifiers, surfactants, and co-surfactants (Schwarz and others 2000; Shahidi and Zhong 2011).

Synergists and antagonists

The effect of different compounds on the rate of lipid oxidation has been discussed recently (Budilarto and Kamal-Eldin 2015a, b). In general, certain surfactant molecules can be classified according to the empirical HLB system with a scale reaching from 1 (highest lipophilic property) to 20 (highest hydrophilic property). The HLB system, however, may not apply for proteins and other complex molecules. When amphiphilic substances are present in the oils and when certain conditions are fulfilled, they will organize spontaneously with other molecules to form micelles and other

types of aggregates in which the polar head groups are directed towards a water interface in the microemulsion defined according to Danielson and Lindman (1981). Minor lipid components such as mono- and di- acylglycerols (HLB = 3 to 5), phospholipids (HLB = 3 to 4), and tocopherols (HLB = 6) play a role in modulating the micro emulsion status of oils. It is claimed that a relationship exists between the HLB value of the surfactants present and their catalytic effect on lipid oxidation. Compounds with high (<15) or low (>3) HLB value hardly influence the rate of autoxidation, while surfactants (3 < HLB < 7) may inhibit the reaction rate and surfactants with HLB values (7 < HLB < 13) increase the rate of oxidation. The effect of HLB is related albeit not linearly to CMC for emulsifiers of different structures (Shinoda and Becher 1978). It was suggested that phospholipids enhance the antioxidant activity of α-tocopherol in bulk lipids in the presence of small amount of water by forming microemulsion aggregates that bring the tocopherol closer to the oxidation site (Koga and Terao 1995). The effect of HLB is related albeit not linearly to CMC for emulsifiers of different structures. The effect of emulsifiers and surfactants is also not straight-forward and is complicated by other con-founding interactions, for instance the size of surfactant headgroup (Silvestre and others 2000), interaction between contaminant hydroperoxides in the emulsifiers and trace metal ions, and complex interactions with antioxidants that may also have surfactant effects.

Phospholipids are well known for their synergistic interactions with tocopherols, especially in fish oil preparations, but these interactions are not straight forward and may be complicated by the chemical structures and concentrations of both phospholipids and tocopherols (Hildebrand and others 1984; Hamilton and others 1998; Takenaka and others 2007; Laguerre and others 2010). The unsaponifiable materials in vegetable oils have a wide range of components that might influence the microenvironment in different ways. For example, cholesterol, alkanes, and squalene were suggested to influence the organization of lamellar and inverted hexagonal phases of phospholipids (Takahashi and others 1996). Besides their roles as radical scavengers and/or metal chelators, antioxidants may have surfactant or co-surfactant properties. When more than 1 antioxidant is present with oxidizing lipids, synergism or antagonism might occur due to structural compatibility and concentrations as was shown for the interactions of quercetin, catechin, and other plant phenols with α-tocopherol (Yanishlieva and Kortenska 1989; Becker and others 2007). Thus, HLB is an empirical parameter that can provide an approximate prediction of the surface activity and associated behavior of molecules but other parameters, such as those obtained by molecular dynamic simulations, might provide better predictive information. Employment of pseudophase kinetic modelling in the study of lipid oxidation reactions is foreseen to provide a better prediction of the partitioning and efficacy of chain-breaking antioxidants in multiphase systems derived from association colloid theory (Gu and others 2013).

To conclude this section, the combination of antioxidants, emulsifiers, surfactants, co-surfactants, salts, pH, other molecular species, and temperature interacts in complex ways and modifies the oxidation rates and the critical micelle concentrations in bulk lipids and emulsions, especially during the induction period (Gupta and others 2001; Mateos and others 2003; Ishii and Nii 2005). Antioxidants, synergists, and other co-existing minor lipid components contribute to the colloidal structure of the mixture and affect the lipid oxidation pathway(s) not only by their involvement in chemical reactions but also through physical interactions. Temperature has a profound effect on these interactions and resultant stabilization, such as the effects of antioxidant polarity and concentration on antioxidant effectiveness diminish with increased oxidation temperature (Mateos and others 2003).

Process and Engineering Possibilities

There has been a growing interest in research and development and commercialization of functional food ingredients over the past decade. Increased consumption of n-3 PUFA-rich oils can be achieved by fortifying staple foods such as breads, milk, fruit juices, tortillas, chocolate, spreads and yogurt with these beneficial fatty acids. However, incorporation of n-3 PUFA into foods is restricted by their oxidative instability and the formation of products resulting from the decomposition of hydroperoxides which are either toxic or causing off-flavors that are deemed undesirable by consumers. A major challenge pertinent to lipid oxidation reactions is the inclusion of highly unsaturated fatty acids, such as the n-3 PUFA of marine species and algae, in food products. So far efforts have not been successful to stabilize these lipids in bulk by the mere addition of primary antioxidants and phospholipid synergists despite small improvements. The other approach to prepare stable food ingredients enriched in n-3 PUFA is *via* engineered micro- and nanoemulsion encapsulations aiming to utilize interfacial technologies to exclude oxygen contact with n-3 PUFA and to incorporate antioxidants and other protective agents (Drush and others 2007, 2009; Jin and others 2007; Jafari and others 2008; Walker and others 2015; Ruiz-Ruiz and others 2017).

Micro- and nano-encapsulation technologies can partially prevent oxidation and extends the shelf-life of n-3 fatty acids, offering practical solutions for stabilization and improved delivery of n-3 PUFA in food products (Ruiz-Ruiz and others 2017). Omega-3 fatty acids have been microencapsulated using different encapsulation techniques. So far, spray drying, freeze-drying, complex coacervation, and extrusion are the most commonly used commercial techniques for microencapsulation of n-3 PUFA (Kaushik and others 2014; Anwar and Kunz 2011). Spray-drying is the most common technique to produce microencapsulated food materials. Equipment is readily available and production costs are lower than most other methods. New techniques, such as electrospraying, may provide a milder spraying compared to spray drying that involves use of hot gas in drying (Gómez-Mascaraque and López-Rubio 2016). In spite of the development of the microencapsulation techniques, this process remains far from completely being controlled (Velasco and others 2006, Ruiz-Ruiz and others 2017).

Nano/microencapsulation of n-3 PUFA in any of the above-mentioned forms requires processing and engineering expertise since these techniques do not always produce a product that is more stable than the nonencapsulated form (Encina and others 2016). The encapsulation efficiency and storage stability of n-3 PUFA microcapsules are important considerations in the development of appropriate encapsulation systems. It is affected by different parameters as shown in Figure 4 including the selection of the matrix, emulsifier, and wall material composition (glass transition temperatures, crystallinity, extent of interaction with the core material), the formulation (antioxidants, synergists, n-3 PUFA) and the processing conditions (temperature, pressure, ratio n-3 PUFA/matrix, water activity, oil distribution within the particle, particle size and surface area) (Gharsallaoui and others 2007). A wide range of materials, including plant polysaccharides, proteins, and peptides, are available as effective carriers of n-3 PUFA and co-delivery of other lipid-soluble ingredients (Kaushik and others 2014). In fact, both the size and shape of formed microparticles depend on the materials and methods used to prepare them. Many

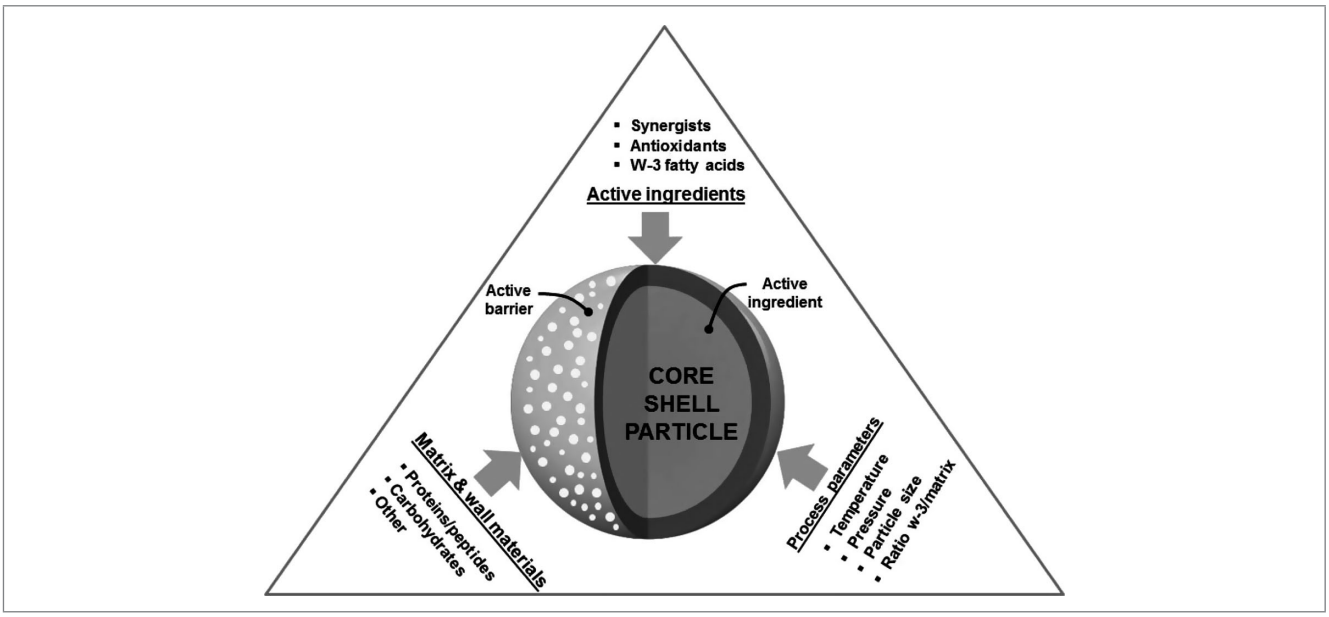

Figure 4–Factors influencing encapsulation efficiency and storage stability of omega-3 oil microcapsules. This depends on the selection of the matrix and wall material composition (glass transition temperatures, crystallinity, and extent of interaction with the core material), the formulation (antioxidants, synergists, n-3 PUFA), and the processing conditions (temperature, pressure, ratio n-3 PUFA/matrix, water activity, oil distribution within the particle, particle size, and surface area, and so on).

different wall materials have been used, such as skim milk powder or mixtures of Na/Ca caseinate with lactose, Maillard reaction products obtained by heat treatments of mixtures of proteins and carbohydrates, sugar beet pectin, gelatin, plant gums, barley protein, and cellulose (Gharsallaoui and others 2007).

During encapsulation of unsaturated fatty acids, it is very important to control the surface free oil, which is widely spread on the surface of microcapsules and exposed to the atmosphere (Velasco and others 2006). The use of multilayer encapsulation and the inclusion of substances such as protein hydrolyzates, gums, and carbohydrate polymers may increase the encapsulation efficacy and add stability to the lipid encapsulates (Shaw and others 2007). The criteria for the selecting a wall material are mainly based on the cost and physicochemical properties such as solubility; infusibility; film forming and emulsifying properties. It was also reported that the use of air as the drying medium at very high temperature produces particles with a porous structure which decreases their shelf-life. Higher total solids content seemed to have a favorable effect on oxidative stability of the microencapsulates and this was attributed to lower contents of occluded air in microcapsules generated from higher solids content microemulsions. Higher homogenization pressures (smaller oil droplet sizes) also may affect the conformation of the proteins causing higher encapsulation efficiencies. The oil-to-wall ratio is very important for oxidative stability of encapsulated n-3 PUFA.

Incorporating antioxidants (EDTA and α-tocopherols) in the microcapsules results in greater stability. The main antioxidative mechanisms necessary to protect microcapsules from oxidation are radical scavenging, metal chelation, and oxygen scavenging. To prevent oxidation reactions of encapsulated n-3 PUFA, it is necessary to combine different approaches, and that, at different stages of processing and conservation of products as shown in Table 1. One of the approaches would be the optimization of oil/fat mixture (fish oils with plant oils and/or fats) to provide maximum stability. Incorporating antioxidants (EDTA and α-tocopherol) is another approach which resulted in microcapsules with greater stability. The main antioxidant mechanisms necessary to protect microcapsules from oxidation are radical scavenging, metal chelation, and oxygen scavenging. Furthermore, the polarity and solubility of an antioxidant determine the actual location of the antioxidant in a given food matrix, which again influences the antioxidant efficacy of the antioxidant (Frankel and others 1994; Gu and others 2013).

The selection and design of emulsifiers have proven to be very important for the stability of bulk lipids and nano- and microemulsions enriched in n-3 fatty acids (Walker and others 2015). The selection of surfactants (nonionic, anionic, cationic, and zwitterion) and emulsifiers (phospholipids, proteins, polysaccharides, saponins, glycolipids) is important not only for the oxidative stability of n-3 fatty acids but also for the physical stability of the microemulsions (Goyal and others 2015; Liu and others 2016; He and others 2017). Different factors may have an opposing effect on the physical structure and oxidative stability of the microemulsions. For example, small droplets enhance the physical stability of microemulsions but adversely affect the oxidizability of fatty acids because of increased surface area (Uluata and others 2015). However, the type of emulsifier(s) and its/their ability to distribute and stabilize the interface is a very important and possibly the most crucial parameter to be considered (Sørensen and others 2007; Horn and others 2013). Different emulsifiers are expected to have different effects on these opposing factors in microemulsions enriched in n-3 fatty acids. Other factors can affect the performance of emulsifiers as, for example, it was found that the effects of sunflower phospholipids is markedly affected by pH and ionic strength (Komaiko and others 2016).

The packaging protocols have an impact on the storage stability of n-3 PUFA microcapsules which may be packed under inert gas, such as nitrogen atmosphere, to extend product's shelf-life. Thus, multivariate statistics considering the above-mentioned parameters may be used efficiently and effectively to provide stable encapsulates of highly unsaturated fatty acids, antioxidants, and

Table 1–Manufacturing strategies aiming to minimize lipid oxidation in bulk lipids and microencapsulates of lipids containing omega-3 fatty acids.

Strategy	Action
1- Select optimal fatty acid composition	Optimize oil/fat mixture to provide maximum stability. Mix fish oils with plant oils and/or fats to achieve the optimal composition.
2- Select optimal primary antioxidant combination	Optimize an antioxidant protection based on optimal composition and concentrations of tocopherol homologues and other possible primary antioxidants of the phenolic type or antioxidant extracts such as rosemary, green tea and so on.
3- Make a smart selection of synergists	Test and select other compounds that may synergize the protective effect of primary antioxidants. Smart combinations including reducing agents (for example, ascorbate), emulsifiers (for example, phospholipids), and other phase modifiers (for example, salts, amino acids, and so on) may help in this regard.
4- Make a smart selection of an inclusion matrix with the aim to minimize surface area and exclude oxygen	Depending on the form of the final product and its purpose, solubility, and other physicochemical attributes, an inclusion matrix may be selected
5- Design a micro-encapsulation strategy considering the wall material and encapsulation method with the aim to minimize surface oil and to maximize solubility	Select wall material and encapsulation method to achieve near 100% encapsulation. There may be a need to further cover the wall with a "glue" of insulating material such as gums. Avoid high temperatures during processing.
6- Select smart packaging strategies and optimize product's shelf-life	Evaluate and optimize smart packaging protocols
7- Use multivariate statistics to achieve the best economical outcome	Use multivariate statistics to achieve the best combination of steps 1 to 6 with focus on cost and economical outcome

synergists, with focus on the cost and best economical outcome. Contemporary knowledge focusing on the significance of the microenvironment for the oxidative stability of n-3 fatty acids will develop to allow a better understanding of the important role of surfactants and emulsifiers in modulating the effects of fatty acid unsaturation and antioxidants. A better mechanistic understanding of the interactions between lipids, antioxidants, other molecular species in the media, and packaging materials/strategies may contribute to the development of functional foods enriched in stabilized n-3 fatty acids.

Conclusions

Our understanding of the lipid oxidation mechanism and the concept of synergism/antagonism has improved by combining the previously established free radical mechanism with different aspects of heterogeneous catalysis by traces metal ions and the effect of micellization. This new paradigm allows for better protection strategies utilizing primary antioxidants and synergists focusing on the prevention of formation as well as scavenging of the lipid hydroperoxides formed during the initiation stage. Based on the available knowledge, smart processing technologies utilizing controlled parameters (temperature and pressure) and proper combinations of primary antioxidants and synergists aiming at controlling the interfacial physics and chemistry are needed for this purpose. Use of low temperature and exclusion of oxygen are important key parameters to be controlled.

The criteria for the selection of the surfactants/co-surfactants for the encapsulation of functional lipids must also include their effects on the oxidative stability of these lipids. For example, the solubility of curcumin in solution was increased by approximately 10 thousand-folds by an optimized formulated encapsulation including vitamin E (3.3% w/w), Tween 20 (53.8% w/w), ethanol (6.6% w/w), and water (36.3% w/w) (Bergonzi and others 2014). In further progress, PUFA-enriched encapsulates may be tailored for the delivery of not only stable nutritional n-3 fatty acids but also other bioactive molecules. It is now the challenge for food engineers to take the next step and develop strategies for stable n-3 PUFA-rich functional ingredients for food applications.

Nomenclature

LOOH	Lipid hydroperoxides
LH	Lipid
$LOO^{\bullet}$	Lipid peroxyl radical
$LO^{\bullet}$	Lipid alkyl radical
$L^{\bullet}$	Lipid radical
$^1O_2$	Singlet state oxygen
XH	Reducing agent
$X^{\bullet}$	Oxidizing radical

Abbreviations

BDE	Bond dissociation energy
BHT	Butylated hydroxyl-toluene
CMC	Critical micelle concentration
DHA	Docosahexaenoic acid
EDTA	Ethylenediaminetetraacetic acid
EPA	Eicosapentaenoic acid
HLB	Hydrophilic lipophilic balance
IP	Induction period
o/w	Oil in water emulsion
PUFA	Polyunsaturated fatty acids

References

Amić D, Davidović-Amić D, Beslo D, Rastija V, Lucić B, Trinajstić N. 2007. SAR and QSAR of the antioxidant activity of flavonoids. Curr Med Chem 14:827–45.

Anwar SH, Kunz B. 2011. The influence of drying methods on the stabilization of fish oil microcapsules: comparison of spray granulation, spray drying, and freeze drying. J Food Eng 105: 367–78.

Astruc D, Lu F, Aranzaes JR. 2005. Nanoparticles as recyclable catalysts: The frontier between homogeneous and heterogeneous catalysis. Angew Chem Intl Ed Engl 44:7852–72.

Baik MY, Suhendro EL, Nawar WW, McClements DJ, Decker EA, Chinachoti P. 2004. Effects of antioxidants and humidity on the oxidative stability of microencapsulated fish oil. J Am Oil Chem Soc 81:355–60.

Barrow C, Wang B, Adhikari B, Liu H. 2013. Spray drying and encapsulation of omega-3 oils. In: Jacobsen C, Nielsen NS, Horn AF, Sorensen M, editors. Food enrichment with omega-3 fatty acids. Oxford, United Kingdom: Woodhead Publishing Ltd. p 194–225.

Bateman L, Hughes H, Morris AL. 1953. Hydroperoxide decomposition in relation to the inhibition of radical chain reactions. Spec Discuss Faraday Soc 14:190–9.

Becker EM, Ntouma G, Skibsted LH. 2007. Synergism and antagonism between quercetin and other chain-breaking antioxidants in lipid systems of increasing structural organization. Food Chem 103: 1288–96.

Bergonzi MC, Hamdouch R, Mazzacuva F, Isacchi B, Bilia, AR. 2014. Optimization, characterization and in vitro evaluation of curcumin microemulsions. LWT – Food Sci Technol 59:148–55.

Berton-Carabin CC, Ropers MH, Genot C. 2014. Lipid oxidation in oil-in-water emulsions: involvement of the interfacial layer. Comp Rev Food Sci Food Safety 13:945–77.

Bolland JL. 1946. Kinetic studies in the chemistry of rubber and related materials. I. The thermal oxidation of ethyl linoleate. Proc R Soc Lond Ser A 186:218–36.

Bolland JL. 1950. Kinetic studies in the chemistry of rubber and related materials. VII. Influence of chemical structure on the α-methylenic reactivity of olefins. Trans Faraday Soc 46:358–68.

Bolland JL, Gee G. 1946a. Kinetic studies in the chemistry of rubber and related materials. II. The kinetics of oxidation of unconjugated olefins. Trans Faraday Soc 42:236–43.

Bolland JL, Gee G. 1946b. Kinetic studies in the chemistry of rubber and related materials. III. Thermochemistry and mechanisms of olefin oxidation. Trans Faraday Soc 42:244–52.

Brimberg UI. 1993. On the kinetics of the autoxidation of fats. J Am Oil Chem. Soc 70:249–54.

Brimberg UI, Kamal-Eldin A. 2003. On the kinetics of the autoxidation of fats: influence of prooxidants, antioxidants and synergists. Eur J Lipid Sci Technol 105:83–91.

Brodnitz MH. 1968. Autoxidation of saturated fatty acids: a review. J Agric Food Chem 16:994–9.

Budilarto ES, Kamal-Eldin A. 2015a. The supramolecular chemistry of lipid oxidation and antioxidation in bulk oils. Eur J Lipid Sci Technol 117:1095–137.

Budilarto ES, Kamal-Eldin A. 2015b. Changes in water content and micelle size during the oxidation of sunflower and canola oils. Eur J Lipid Sci Technol 117:1971–7.

Burch R, Crittle DJ, Hayes MJ. 1999. C–H bond activation in hydrocarbon oxidation on heterogeneous catalysis. Catal Today 47:229–34.

Calder PC. 2013. Nutritional benefits of omega-3 fatty acids. In: Jacobsen NS, Nielsen AF, Horn AD, Sorensen M, editors. Food enrichment with omega-3 fatty acids, C. Cambridge, UK: Woodhead Publishing Ltd.

Chaiyasit W, Elias RJ, McClements DJ, Decker EA. 2007. Role of physical structures in bulk oils on lipid oxidation. Crit Rev Food Sci Nutr 47:299–317.

Chaiyasit W, McClements DJ, Weiss J, Decker EA. 2008. Impact of surface-active compounds on physicochemical and oxidative properties of edible oil. J Agric Food Chem 56:550–6.

Champagne CP, Fustier P. 2007. Microencapsulation for the improved delivery of bioactive compounds into foods. Curr Opin Biotechnol 18:184–90.

Chan HWS. 1987. The mechanisms of autoxidation. In: Chan HWS, editor. Autoxidation of unsaturated lipids, London: Academic Press. p 141–206.

Chen B, Han A, McClements DJ, Decker EA. 2010. Physical structures in soybean oil and their impact on lipid oxidation. J Agric Food Chem 58:11993–9.

Chen B, Han A, Laguerre M, McClements DJ, Decker EA. 2011a. Role of reverse micelles on lipid oxidation in bulk oils: impact of phospholipids on antioxidant activity of α-tocopherol and Trolox. Food Funct 2:302–9.

Chen B, McClements DJ, Decker EA. 2011b. Minor components in food oils: a critical review of their roles on lipid oxidation chemistry in bulk oils and emulsions. Crit Rev Food Sci Nutr 51:901–6.

Chen B, Panya A, McClements DJ, Decker EA. 2012. New insights into the role of iron in the promotion of lipid oxidation in bulk oils containing reverse micelles. J Agric Food Chem 60:3524–32.

Chen H, Le DJ, Schanus EG. 1992. The inhibitory effect of water on the Co^{2+} and Cu^{2+}-catalyzed decomposition of methyl linoleate hydroperoxides. Lipids 27:234–89.

Cheng Z, Li Y. 2007. What is responsible for the initiating chemistry of iron-mediated lipid peroxidation: an update. Chem Rev 107:748–66.

Choe E, Min DB. 2007. Chemistry of deep fat frying oils. J Food Sci 72, R77–86.

Cho SY, Miyashita K, Miyazawa T, Fujimoto K, Kaneda T. 1987. Autoxidation of ethyl eicosapentaenoate and docosahexaenoate. J Am Chem Soc 64:876–9.

Dalby T, Care CM. 1999. Rosenbluth chain cluster growth in the study of micelle self-assembly. Phys Rev 59:6152–60.

Danielson I, Lindman B. 1981. The definition of microemulsion. Colloids Surf 3:392–3.

Drusch S, Mannino S. 2009. Patent-based review on industrial approaches for the microencapsulation of oils rich in polyunsaturated fatty acids. Trends Food Sci Technol 20:237–44.

Drusch S, Serfert Y, Scampicchio M, Schmidt-Hansberg B, Schwarz K. 2007. Impact of physicochemical characteristics on the oxidative stability of fish oil microencapsulated by spray-drying. J Agric Food Chem 55:11044–51.

Encina C, Vergara C, Gimenéz B, Oyarzún-Ampuero F, Robert P. 2016. Conventional spray-drying and future trends for the microencapsulation of fish oil. Trends Food Sci Technol 56:46–60.

Farmer EH, Sundralingam A. 1942. The course of autoxidation reactions in polyisoprene and allied compounds I. The structure and reactive tendencies of the peroxides of simple olefins. J Chem Soc 1942:121-39.

Farmer EH, Sutton DA. 1943. The course of autoxidation reactions in polyisoprenes and allied compounds. V. Observations on fish-oil acids. J Chem Soc 1943:122–5.

Farmer EH, Sutton DA. 1946. The course of autoxidation reactions in polyisoprenes and allied compounds. XI. Double bond movement during the autoxidation of a mono-olefin. J Chem Soc 1946:10–3.

Feuell AJ, Skellon JH. 1952. The oxidation of monoethenoid fatty acids and esters. J Chem Soc 1952:59–62.

Frankel EN, Huang SW, Kanner J, German JB. 1994. Interfacial phenomena in the evaluation of antioxidants: bulk oils vs emulsions. J Agric Food Chem 42:1054–9.

Gharsallaoui A, Roudaut G, Chambin O, Voilley A, Saurel R. 2007. Applications of spray-drying in microencapsulation of food ingredients: an overview. Food Res Intl 40:1107–21.

Glickman MH, Klinman JP. 1995. Nature of rate-limiting steps in the soybean lipoxygenase-1 reaction. Biochem. 34:14077–92.

Gómez-Mascaraque L, López-Rubio A. 2016. Protein-based emulsion electrosprayed micro- and submicroparticles for the encapsulation and stabilization of thermosensitive hydrophobic bioactives. J Colloid Interface Sci 465:259–70.

Gopala-Krishna AG, Prabhakar JV. 1992. Effect of water activity on secondary products formation in autoxidizing methyl linoleate. J Am Oil Chem Soc 69:178–83.

Gopala-Krishna AG, Prabhakar JV. 1995. Retarding autoxidation in raw peanut oil by addition of water. J Am Oil Chem Soc 72:1219–21.

Goyal A, Sharma V, Upadhyay N, Singh AK, Arora S, Lal D, Sabikhi L. 2015. Development of stable flaxseed oil emulsions as a potential delivery system for ω-3 fatty acids. J Food Sci Technol 52:4256–65.

Gu Q, Bravo-Diaz C, Romsted LS. 2013. Using the pseudophase kinetic model to interpret chemical reactivity in ionic emulsions: determining antioxidant partition constants and interfacial rate constants. J Colloid Interface Sci 400:41–8.

Gupta R, Moralidhara HS, Davis HT. 2001. Structure and phase behavior of phospholipid-based micelles in non-aqueous media. Langmuir 17: 5176–83.

Gülçin I. 2006. Antioxidant activity of caffeic acid (3,4-dihydroxycinnamic acid). Toxicol 217:213–20.

Hall III C. 2001. Sources of natural antioxidants: oilseeds, nuts, cereals, legumes, animal products and microbial sources. In: Pokorny J, Yanishlieva N, Gordon M, editors. Antioxidants in food: practical applications. England: Woodhead Publishing. p 159–209.

Hamilton RJ, Kalu C, McNeill GP, Padley FB, Pierce JH. 1998. Effect of tocopherols, ascorbyl palmitate, and lecithin on autoxidation of fish oil. J Am Oil Chem Soc 75:813–22.

He Z, Zeng W, Zhu X, Zhao H, Lu Y, Lu Z. 2017. Influence of surfactin on physical and oxidative stability of microemulsions with docosahexaenoic acid. Colloids Surf B 151:232–9.

Hess PS, O'Hare GA. 1950. Oxidation of linseed oil – temperature effects. Ind Eng Chem 42:1424–31.

Heidelbaugh ND, Karel M. 1970. Effect of water binding agents on the catalyzed oxidation of methyl linoleate. J Am Oil Chem Soc 47: 539–44.

Hildebrand DH, Terao J, Kito M. 1984. Phospholipids plus tocopherols increase soybean oil stability. J Am Oil Chem Soc 61:552–55.

Holman RT, Elmer OC. 1947. The rates of oxidation of unsaturated fatty acids and esters. J Am Oil Chem Soc 24:127-9.

Horn AF, Barouh N, Nielsen NS, Baron CP, Jacobsen C. 2013. Homogenization pressure and temperature affect composition of proteins in the aqueous phase and oxidative stability of fish oil-in-water emulsions. J Am Oil Chem Soc 90:1541–50.

Huang S-W, Frankel EN, German JB. 1994. Antioxidant activity of α- and γ-tocopherol in bulk oils and in oil-in-water emulsion. J Agric Food Chem 42:2108–14.

Ishii F, Nii T. 2005. Properties of various phospholipid mixtures as emulsifiers or dispersing agents in nanoparticle drug carrier preparations. Colloids Surf B 41:257–62.

Jacobsen C. 2015. Some strategies for the stabilization of long chain n-3 PUFA-enriched foods: a review. Eur J Lipid Sci Technol 117:1853–66.

Jafari SM, Assadpoor E, Bhandari B, He Y. 2008. Nano-particle encapsulation of fish oil by spray drying. Food Res Intl 4:172–83.

Jin Y, Perrie C, Zhang W, Diepen CV, Curtis J, Barrow CJ. 2007. Microencapsulation of marine lipids as a vehicle for functional food delivery. In: Barrow C, Shahidi F, editors. Marine nutraceuticals and functional foods, CRC Press: Boca Raton. p 115–54.

Kamal-Eldin A, Appelqvist L-A. 1996. The chemistry and antioxidant properties of tocopherols and tocotrienols. Lipids 31:671–701.

Kamal-Eldin A. 2006. Effect of fatty acid composition and tocopherol content on the oxidative stability of vegetable oils. Eur J Lipid Sci Technol 58:1051–61.

Kamal-Eldin A, Budilarto E. 2015a. Tocopherols and tocotrienols as antioxidants for food preservation. In: Shahidi F, editor. Handbook of antioxidants for food preservation. Chapter 6. Woodhead Publishing Series in Food Science, Technology and Nutrition Series. p 141–54.

Kaushik P, Dowling K, Barrow CJ, Adhikari B. 2014. Microencapsulation of omega-3 fatty acids: a review of microencapsulation and characterization methods. J Funct Foods 19:868–81.

Kern VW, Willersinn H. 1955. Über die autoxydation ungesättigter verbindungen. III. Die katalyse der autoxydation des linolsäremethylesters durch metallverbindungen und durch kombinierte katalysatorsysteme. Makromol chem 15:36–59.

Koga T, Terao J. 1995. Phospholipids increase radical-scavenging activity of vitamin E in a bulk oil model system. J Agric Food Chem 43: 1450–4.

Kagan VE, Serbinova EA, Bokalova RA. Stoytchev TS, Erin AN, Prilipko LL, Evstigneeva RP. 1990. Mechanisms of stabilization of biomembranes by alpha-tocopherol: The role of hydrocarbon chain in the inhibition of lipid peroxidation. Biochem Pharmacol 40:2403–13.

Komaiko J, Sastrosubroto A, McClements DJ. 2016. Encapsulation of w-3 fatty acids in nanoemulsion-based delivery systems fabricated from natural emulsifiers: sunflower phospholipids. Food Chem 203:331–9.

Labuza TP, Dugan Jr. LR. 1971. Kinetics of lipid oxidation in foods. Crit Rev Food Technol 2:355–405.

Labuza TP, Silver M, Cohn M, Heidelbaugh ND, Karel M. 1971. Metal-catalyzed oxidation in the presence of water in foods. J Am Oil Chem Soc 48:527–31.

Laguerre M, Giraldo LJ, Lecomte J, Figueroa-Espinoza MC, Baréa B, Weiss J, Decker EA, Villeneuve P. 2009. Chain length affects antioxidant properties of chlorogenate esters in emulsion: the cutoff theory behind the polar paradox. J Agric Food Chem 57:11335–42.

Laguerre M, Chen B, Lecomte J, Villeneuve P, McClements DJ, Decker EA. 2010. Antioxidant properties of chlorogenic acid and its alkyl esters in stripped corn oil in combination with phospholipids and/or water. J Agric Food Chem 59:10361–6.

Laguerre M, Bayrasy C, Panya A, Weiss J, McClements DJ, Lecomte J, Decker EA, Villeneuve P. 2015. What makes good antioxidants in lipid-based systems? The next theories beyond the polar paradox. Crit Rev Food Sci Nutr 55:183–201.

Laguerre M, Bily A, Roller M, Birtić S. 2017. Mass transport phenomena in lipid oxidation and antioxidation. Ann Rev Food Sci Technol 8:391–411.

Liavonchanka A, Feussner I. 2006. Lipoxygenases: occurrence, functions and catalysis. J Plant Phys 163:348–57.

Liu F, Zhu Z, Ma C, Luo X, Bai L, Decker EA, Gao Y, McClements DJ. 2016. Fabrication of concentrated fish oil emulsions using dual-channel microfluidization: Impact of droplet concentration on physical properties and lipid oxidation. J Agric Food Chem 64:9532–41.

Llorent-Martinez EJ, Ortega-Barrales P, Fernández-de Córdova ML, Dominquez-Vidal A, Ruiz-Medina A. 2011. Investigation by ICP-MS of trace element levels in vegetable edible oils produced in Spain. Food Chem 122:1257–62.

Lombrado D, Kiselev MA, Magazu S, Calandra P. 2015. Amphiphiles self-assembly: Basic concepts and future perspectives of supramolecular approaches. Adv Cond Matter Phys 2015. https://doi.org/10.1155/2015/151683.

Mateos R, Dominguez MM, Espartero JL, Cert A. 2003. Antioxidant effect of phenolic compounds: α-tocopherol and other minor components in olive oil. J Agric Food Chem 51:7170–5.

Mikhailov AS. 1999. Nonlinear phenomena in heterogeneous catalysis. Physics A 263:329–37.

Miyashita K, Frankel EN, Neff WE, Awl RA. 1990. Autoxidation of polyunsaturated triacylglycerols. III. Synthetic triacylglycerols containing linoleate and linolenate. Lipids 25:48–53.

Miyashita K. 2014. Paradox of omega-3 PUFA oxidation. Eur J Lipid Sci Technol 116:1268–79.

Moulik SP. 1996. Micelles: self-organized surfactants. Curr Sci 71:368–76.

Neff WE, El-Agaimy M. 1996. Effect of linoleic acid position in triacylglycerols on their oxidative stability. LWT – Food Sci Technol 29:772–5.

Noguchi N, Yamashita H, Hamahara J, Nakamura A, Kühn H, Niki E. 2005. The specificity of lipoxygenase-catalyzed lipid peroxidation and the effects of radical-scavenging antioxidants. Biol Chem 383:619–26.

Paízková H, Pokorný J, Davídek J, Kmínek M. 1989. Effect of polar substances on the decomposition of hydroperoxy oleate on heating. Nahrung 33:477–9.

Porter WL. 1993. Paradoxical behavior of antioxidants in food and biological systems. In: Williams GM, editor. Antioxidants: chemical, physiological, nutritional and toxicological aspects. Princeton, Princeton Scientific, NJ, USA. p 93–122

Privett OS, Blank ML. 1962. The initial stages of auto-oxidation. J Am Oil Chem Soc 39:465–9.

Ramanathan M, Shrestha LK, Mori T, Ji Q, Hill JP, Ariga K. 2013. Amphiphile nanoarchitectonics: from basic physical chemistry to advanced applications. Phys Chem Chem Phys 15: 10580–611.

Ruiz-Ruiz JC, Ortiz-Vazquez EL, Segura-Campos MR. 2017. Encapsulation of vegetable oils as source of omega-3 fatty acids for enriched functional foods. Crit Rev Food Sci Nutr 57:1423–34.

Russell GA. 1957. Deuterium-isotope effects in the autoxidation of aralkyl hydrocarbons—mechanism of the interaction of peroxy radicals. J Am Oil Chem Soc 79:3871–7.

Schaich KM. 1992. Metals and lipid oxidation: contemporary issues. Lipids 27:209–18.

Schaich KM. 2012. Thinking outside the classical chain reaction box of lipid oxidation. Lipid Tech 24:55–8.

Schilstra MJ, Veldink GA, Vliegenthart JF. 1993. Kinetic analysis of the induction period in lipoxygenase catalysis. Biochem 32:7686–91.

Schneider C, Pratt DA, Porter NA, Brash AR. 2007. Control of oxygenation in lipoxygenase and cyclooxygenase catalysis. Chem Biol 14:473–88.

Schwarz K, Huang S-W, German JB, Tiersch B, Hartmann J, Frankel EN. 2000. Activities of antioxidants are affected by colloidal properties of oil-in-water and water-in-oil emulsions and bulk oils. J Agric Food Chem 48: 4874–82.

Shahidi F, Zhong Y. 2011. Revisiting the polar paradox theory: a critical overview. J Agric Food Chem 59:3499–504.

Shaw LA, McClements DJ, Decker EA. 2007. Spray-dried multilayered emulsions as a delivery method for omega-3 fatty acids into food systems. J Agric Food Chem 55:3112–9.

Shinoda K, Becher P. 1978. Principles of solution and solubility. New York: Marcel Dekker.

Silva MM, Santos MR, Caroco G, Rocha R, Justino G, Mira L. 2002. Structure-antioxidant activity relationships of flavonoids: a re-examination. Free Radic Res 36:1219–27.

Silvestre MPC, Chaiyasit W, Brannan RG, McClements DJ, Decker EA. 2000. Ability of surfactant headgroup size to alter lipid and antioxidant oxidation oil-in-water emulsion. J Agric Food Chem 48:2057–61.

Sørensen A-DM, Baron CP, Let MB, Brüggemann DA, Pedersen LRL, Jacobsen C 2007. Homogenization conditions affects the oxidative stability of fish oil enriched milk emulsions: oxidation linked to changes in the protein composition at the oil-water interface. J Agric Food Chem 55:1781–9.

Spranger T, Finckh B, Fingerhut R, Kohlschütter A, Beisiegel U, Kontush A. 1998. How different constituents of human plasma and low density lipoprotein determine plasma oxidizability by copper. Chem Phys Lipids 91:39–52.

Stupp SI, LeBonheur VV, Walker K, Li LS, Huggins KE, Keser M, Armstutz A. 1997. Supramolecular materials: self-organized nanostructures. Science 276:384–9.

Sullivan JC, Budge SM, St-Onge M. 2011. Modelling the primary oxidation in commercial fish oil preparations. Lipids 46:87–93.

Takahashi H, Sinoda K, Hatta I. 1996. Effects of cholesterol on the lamellar and the inverted hexagonal phases of dielaidoylphosphatidylethanolamine. Biochim Biophys Acta 1289:209–16.

Takenaka A, Hosokawa M, Miyashita K. 2007. Unsaturated phosphatidylethanolamine as effective synergist in combination with α-tocopherol. J Oleo Sci 56:511–6.

Tavadyan L, Khachoyan A, Martoyan G, Kamal-Eldin A. 2007. Numerical revelation of the kinetic significance of individual steps in the reaction mechanism of methyl linoleate peroxidation inhibited by α-tocopherol. Chem Phys Lipids 147:30–45.

Torres de Pinedo A, Penalver P, Morales JC. 2007. Synthesis and evaluation of new phenolic-based antioxidants: structure-activity relationship. Food Chem 103:55–61.

Tretyakov YD. 2003. Self-organization processes in the chemistry of materials. Russ Chem Rev 72:651–79.

Uluata S, McClements DJ, Decker EA. 2015. Physical stability, autoxidation, and photosensitized oxidation of ω-3 oils in nanoemulsions prepared with neutral and synthetic surfactants. J Agric Food Chem 63:9333–40.

Velasco J, Marmesat S, Dobarganes C, Márquez-Ruiz G 2006. Heterogeneous aspects of lipid oxidation in dried microencapsulated oils. J Agric Food Chem 54:1722–9.

Veldink GA. 1994. Kinetic analysis of the induction period in lipoxygenase catalysis. Biochem 32:7686-91.

Walker R, Decker EA, McClements DJ. 2015. Development of food-grade nanoemulsions and emulsions for delivery of omega-3 fatty acids: opportunities and obstacles in the food industry. Food Funct 6:42–55.

Waller TM, Decker I, Frisch JP, Kernstock RM, Kim YW, Funck MO Jr. 2008. Secondary alkyl hydroperoxides as inhibitors and alternate substrates for lipoxygenase. Biochem 47:331–8.

Wang ZX, Killilea SD, Srivastava DK. 1993. Kinetic evaluation of substrate-dependent origin of the lag phase in soybean lipoxygenase-I catalyzed reactions. Biochem 32:1500–9.

Wijesundera C, Ceccato C, Watkins P, Fagan P, Fraser B, Thienthong N, Perlmutter P. 2008. Docosahexaenoic acid is more stable to oxidation when located at the sn-2 position of triacylglycerol compared to sn-1(3). J Am Chem Soc 85:543–8.

Yanishlieva NV, Kortenska VD. 1989. On the participation of fatty alcohols in the autoxidation of lipids. J Sci Food Agric 47:215-23.

Yanishlieva NV, Marinova EM. 1992. Inhibited oxidation of lipids I: complex estimation and comparison of the antioxidative properties of some natural and synthetic antioxidants. Eur J Lipid Sci Technol 94:374–9.

Yanishlieva NV, Kamal-Eldin A, Marinova EM, Toneva AG. 2002. Kinetics of antioxidant action of α- and γ-tocopherols in sunflower and soybean triacylglycerols. Eur J Lipid Sci Technol 104:262–70.

Yazu K, Yamamoto Y, Niki E, Miki K, Ukegawa K. 1998. Mechanism of lower oxidizability of eicosapentaenoate than linoleate in aqueous micelles. II. Effect of antioxidants. Lipids 33:597–00.

Xenakis A, Papadimitriou V, Sotiroudis TG. 2010. Colloidal structures in natural oils. Curr Opin Colloid Interface Sci 15:55–60.