Chapter 10
Nanoemulsions: Industrial Production and Food-Grade Applications

Sonal Agarwal, Swathika Vivekanandan, Trisha David, Mahima Mitra, Jeyanthi Palanivelu, and Ramalingam Chidambaram

Abstract The heterogeneous dispersion of two immiscible liquids forming a metastable system, with sizes ranging from 20 to 1000 nm generate nanoemulsions. Nanoemulsions are capable of efficiently delivering bioactive and flavoring molecules by crossing biological obstruction. These polymer systems in the food industry are designed to maintain the functionality of the active ingredients such as digestibility and antioxidant, anti-inflammatory and antimicrobial properties. A nanoemulsion maintains profitable concerns over conventional systems due to its high optical clarity, surface area, surface reactivity, good physical stability and better bioavailability of the substances that are encapsulated. Nanoemulsions can be produced by low and high energy methods, but there is a substantial interest towards low energy methods, since the latter are suitable to produce beverages such as soft drinks or fortified water, since the final product contains relatively less amount of surfactant. These systems can also serve as an effective platform for the incorporation of nutrients, nutraceuticals and vitamins. The objective of this chapter was to analyze the different methods of production of nanoemulsions, in particular the low energy methods and the applications of food grade nanoemulsions.

Keywords Bioactive molecule · Bioavailability · Low energy method · Nutraceuticals

10.1 Introduction

The introduction of nanotechnology into food industry was marked in late 1800's during the discovery of pasteurization process by Louis Pasteur. The first revolutionary step made in food industry was to improve the stability of the packed and un-packed food by its bactericidal action, to prevent food spoilage and maintain

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food quality (Chellaram et al. 2014). Recent survey suggests researcher's interest towards the advancements in nanotechnology due to its potential applications in various domains/industries. The various ways in which nanotechnology is applicable in the food industry includes agriculture, food processing and packaging (Gutiérrez and Alvarez 2018; Gutiérrez 2018a; Toro-Márquez et al. 2018; Merino et al. 2018; Gutiérrez et al. 2019; Merino et al. 2019). The derivatives of nanotechnology which found its application in food industry are nanocapsules, nanotubes, nanoparticles, nanosensors, nanofilms, nanoclays and nanoemulsions (Gutiérrez et al. 2017). Of these, there is a substantial interest in the application of nanoemulsions in food processing, since it is a potential tool for formulating new food products (Odriozola-Serrano et al. 2014; Gutiérrez and Álvarez 2017). They ensure the stability of food products during manufacturing, processing, packaging and shipping; deliver functional ingredients with beneficial activities to specific sites of action; improve food security without disturbing the environment and; are new and effective material for pathogen detection (Abdullaeva 2017). Nanoemulsions are kinetically stable and thermodynamically unstable colloidal dispersions (Komaiko and McClements 2014; Guttoff et al. 2015; Karthik et al. 2017; Walia et al. 2017). They are optically clear and can increase the chemical stability, improve bioavailability as well as increase the absorption of bioactive agents that are encapsulated (Odriozola-Serrano et al. 2014; Komaiko and McClements 2014). Nanoemulsions can be broadly categorized into oil-in-water (O/W) nanoemulsions or water-in-oil (W/O) nanoemulsions (Fig. 10.1 and Fig. 10.2), of which O/W nanoemulsions are

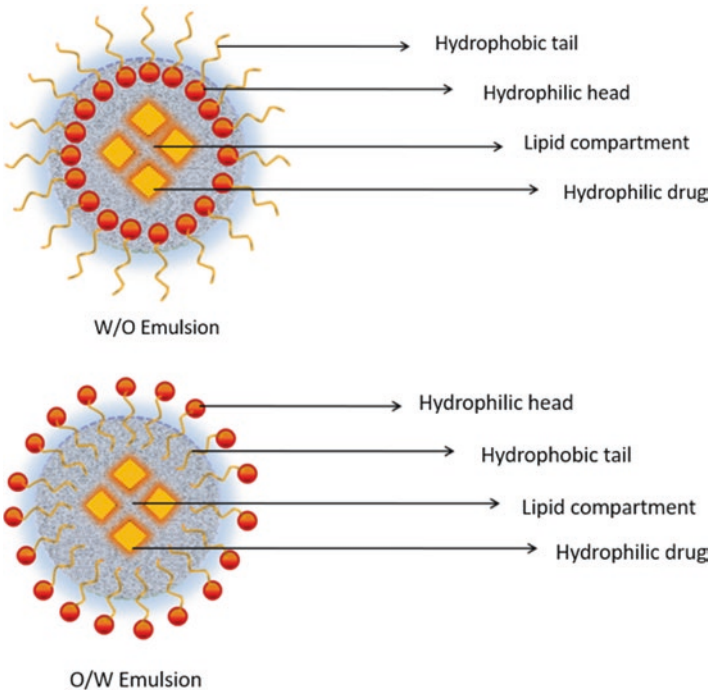

Fig. 10.1 Structure and composition of water-in-oil (W/O) and oil-in-water (O/W) nanoemulsions

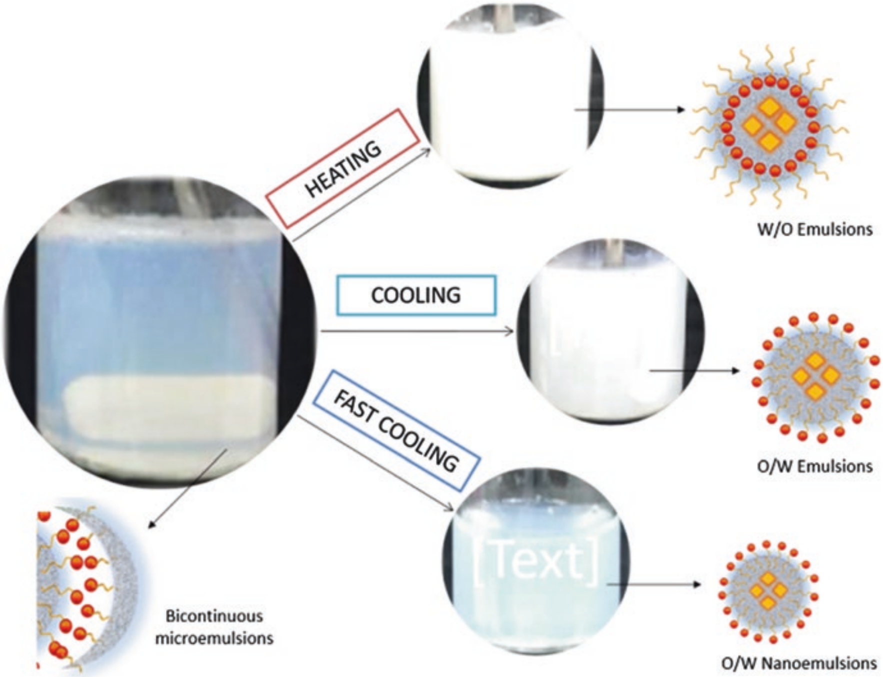

Fig. 10.2 Fabrication of nanoemulsions

commonly used in food industry (Walia et al. 2017). Nanoemulsions are produced by both low and high energy methods (Fig. 10.3) (Gutiérrez 2018b). However, food-grade nanoemulsions are fabricated through low energy techniques (Homs et al. 2018). Nanoemulsions will be selected for applications in food industry based on their performance, safety, commercial viability, robustness, and food-matrix compatibility (McClements 2015; Abdullaeva 2017). The objective of this chapter was thus to analyze the various production methods, in particular low energy methods and applications of food-grade nanoemulsions.

10.2 Properties and Characteristics of Nanoemulsions

10.2.1 Properties of Nanoemulsions

Nanoemulsion droplet sizes ranges from 50 to 1000 nm, but droplets of 20–200 nm forms stable liquid-in-liquid dispersions and 10–100 nm sized droplets are known to have applications in food industry (Lorenzo et al. 2018). They are heterogeneous dispersion mixture of two immiscible liquids, i.e. W/O or O/W (McClements 2012; Komaiko and McClements 2016). Nanoemulsions appear transparent as their sizes are significantly smaller than the wavelength of visible light, thus acting as the

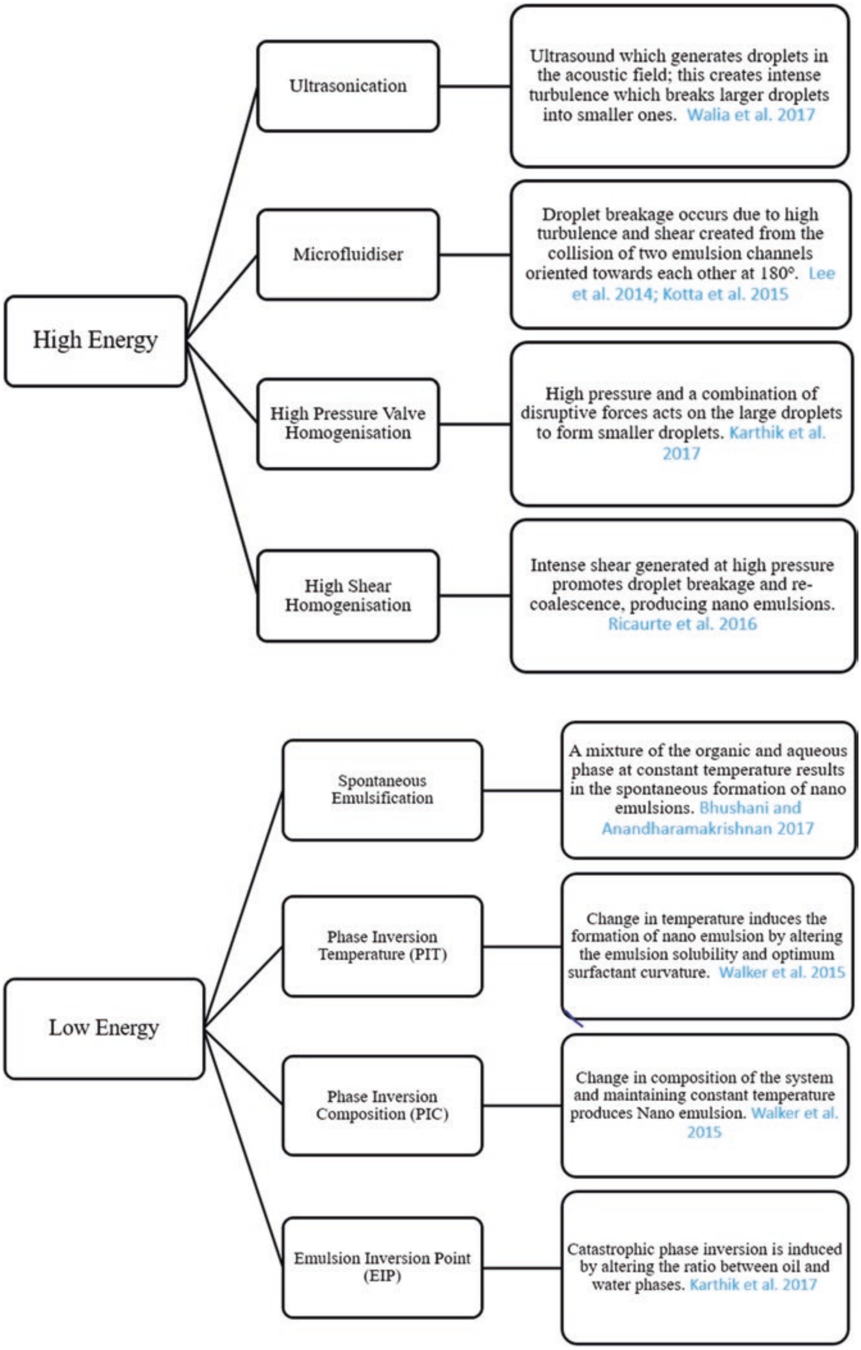

Fig. 10.3 Classification of nanoemulsion production techniques

ideal component to be opted in the food industry (Gupta et al. 2016). The size plays an important role, since it affects properties such as biological activity, encapsulation and release characteristics and optical clarity (Joye et al. 2014).

The small size property of nanoemulsions has many advantages such as extreme resistance to deformation, resulting partly in kinetic stability, the high surface-to-volume ratio of nanoemulsions improves its encapsulated component bioavailability and reactivity, increased surface area eases transportation through the plasma membrane (Helgeson 2016) and increases the enzyme activity at the oil-water interface. Small particles have the ability to cross the mucous layer and get absorbed by the epithelium cells. This leads to faster lipid digestion (Salvia-Trujillo et al. 2013; Walker et al. 2015).

The properties of nanoemulsions include optically transparent appearance, high surface area per unit volume, tunable rheology and robust stability. Nanoemulsions have lower sensitivity towards dilution, changes in pH and temperature when compared to other emulsions (Gupta et al. 2016). They can be designed to have different optical, rheological and stability properties by controlling their compositions and structures.

Optical properties: Optical properties refer to the visual appearance of the nanoemulsion. It is important that the optical properties of nanoemulsions are controlled because food industry incorporates lipophilic bioactive compounds (vitamins and nutraceuticals) into optically transparent delivery systems (Ricaurte et al. 2016). If nanoemulsions are optically opaque, then this attribute is less important. Optical properties can be altered by droplet size, droplet concentration and refractive index contrast. The optical property of nanoemulsions is inversely proportional to its radius size. Example, droplets with radius less than 40 nm appear transparent and translucent whereas when the droplet radius is approximately between 40 and 60 nm, they appear turbid or opaque (McClements 2013).

Rheological properties: From the rheological perspective, nanoemulsions exhibit stronger elasticity compared to other emulsions, thus providing better healing behavior (Gupta et al. 2016). Nanoemulsions intended to deliver lipophilic bioactive compounds in fortified water or soft drinks should not increase the viscosity ideally. However, for some functional food products such as yogurts, sauces and so on it is desirable to have a highly viscous or gel-like material (McClements 2013).

Physical stability: Nanoemulsion stability depends on its composition and structure, and is influenced by various environmental conditions it experiences within a product including mechanical agitation, thermal processing, transportation, freezing, dehydration and storage conditions (Gupta et al. 2016; Dizaj et al. 2016). Most nanoemulsions are physically stable and ensure the dominance of Brownian motion over gravitational force, thus forming a homogenized suspension (Helgeson 2016). The destabilization mechanisms which can break the metastable system are mainly creaming, flocculation, Ostwald ripening and coalescence (McClements 2012). In creaming, droplets rise up, leading to phase separation. If the droplets are denser, they tend to move downwards leading to sedimentation. In flocculation, the droplets approach each other due to attractive interactions, and move as a single entity.

Ostwald ripening, more prevalent in nanoemulsions, occurs due to the difference in chemical potential of solute within droplets of different size. Coalescence involves droplets merging together and forming a larger drop. It is often difficult to differentiate between flocculation and coalescence in an emulsion (Gupta et al. 2016).

Chemical stability: Light-catalyzed reactions may occur more rapidly in transparent nanoemulsions. Surface-catalyzed reactions, such as lipid oxidation or lipase digestion tend to occur more rapidly. Nanoemulsions are isotropic, so they retain a relatively high kinetic stability for a longer duration and, therefore, ideal nanoemulsion systems must retard any potential chemical degradation reactions (McClements 2013). Due to the ability of the solidified lipid phase to inhibit molecular diffusion processes, solid liquid nanoemulsions may be able to protect encapsulated lipophilic components from chemical degradation by lipid crystallization of lipophilic component (Joye et al. 2014).

The polarity property defines the interaction of the nanoemulsion or nanoparticles in the biological system. Another property of nanoemulsions is digestibility, which depends on the core shell structure composition (McClements 2013). As the degree of unsaturation decreases, the digestion becomes easy (McClements 2013).

10.2.2 Characteristics of Nanoemulsions

Nanoemulsions can be characterized based on their size, pH, components compatibility, content uniformity, density, conductivity and surface tension (Dizaj et al. 2016). Nanoemulsions are nanoscale delivery systems which are formulated to ensure their safety, economic viability and effectiveness. For application of nanoemulsion based delivery system in food industry, number of characteristics is to be considered specifically (McClements 2015).

10.2.3 Various Characteristic Features of a Nanoemulsion to be Used in Food

The robustness of a nanoemulsion is important to maintain its chemical and physical stability even when exposed to external factors such as environmental stress. It must also preserve its desirable functional attributes.

Nanoemulsions must be commercially available to manufacture the food grade ingredients with these delivery systems and also the processing methods that are economically viable. High loading capacity is desired to be capable for encapsulating a significant quantity of the bioactive ingredient within the system.

Active compound retention and improved bioavailability: They should be able to encapsulate the active form of the compound until its delivery to site of action. It should be able to increase the chemical stability of the encapsulated compounds during its processing, digestion in gastrointestinal tract or storage.

Food matrix compatibility: The encapsulated bioactive agent should be capable of being homogenized into the final food product with no damage to its distinctive characteristics. It should mask the off-flavor, off-odor and after taste of the encapsulated bioactive compound. The encapsulated bioactive agent should also be compatible with food matrix or beverage in which it has been fortified and it should not affect the sensory characteristic and overall acceptance of the food (Bhushani and Anandharamakrishnan 2017; McClements 2015).

Safety

Safety of nanoemulsions is an important characteristic required for its use in the food industry. If nanoemulsions are completely digested inside the gastrointestinal tract (GIT) as a result giving products of digestion that are same as those which are formed by larger particles and are formed at a similar site, then they are expected to be more toxic. However, if nanoemulsions are not digested completely, or if they are forming products of digestion that are very dissimilar, or are being digested in different regions of the GIT as compared to the bigger particles, then there might be few concerns relating to toxicity. Therefore, potential toxicity testing of the food-grade nanoemulsions stands great importance (McClements 2013).

10.3 Delivery Systems

The physical stability of food-grade nanoemulsions as it passes through the path that includes the mouth, stomach and small intestine depends upon the emulsifier used (Shu et al. 2018). The four mechanisms through which emulsifiers stabilize nanoemulsions are electrostatic, steric, electrosteric and electrostatic-steric mechanisms. Emulsifiers adsorb onto the surface of the droplets acting as a barrier for the protection of nano-sized droplets from coalescence and aggregation during emulsification process and storage (Shariffa et al. 2016). An ideal emulsifier must exhibit the following properties: surface activity, adsorption kinetics, interfacial tension reduction, stabilization and surface coverage to produce nanoemulsions with smaller droplet size during homogenization. Structure of emulsifiers influences the emulsifying and stabilizing mechanisms (Ozturk and McClements 2016). Based on the type of emulsifiers used, food-grade nanoemulsion delivery systems can be divided into three groups: lipid-based nanosystems, surfactant-based nanosystems and biopolymer-based nanosystems (Table 10.1) (Bhushani and Anandharamakrishnan 2017).

10.3.1 Lipid-Based Nanosystems

Lipid-based nanoemulsions incorporated with bioactive compounds improves the solubility property of active compounds, improves bioavailability, chemical and gastrointestinal stability (Yang and McClements 2013; Bhushani and Anandharamakrishnan 2017). Lipid-based emulsifier such as lecithin is commonly

Table 10.1 Different types of delivery systems: Properties and characteristics

Types of emulsifier	Optical characteristics	Factors that affect stability	Emulsifier properties	Examples	Reference
Surfactant	Optically clear.	Temperature.	Thermodynamically stable, have low toxicity and lack of irritability.	Tween 20, 40, 60, 80, 85 and Polysorbate 20, 28, 80.	Sugumar et al. (2013); Dizaj et al. (2016)
Lipid	Ranges from clear to opaque depending upon their size.	pH, ionic strength and temperature.	Have low solubility, low toxicity, high intestinal permeability, high encapsulation efficiency and strong electrostatic repulsion.	Lecithin, phosphated mono- and diglycerides.	Ozturk and McClements (2016)
Biopolymer	Ranges from clear to opaque depending upon their particle refractive index and size.	pH, temperature, ionic strength and metal chelating agents.	Exhibit specific interfacial behavior, high loading capability and response to environmental stresses.	Nanofibers, starch, cellulose, citrus pectin, guar gum, alginate, chitosan and dextran. Amphiphilic proteins such as casein, lactoferrin, β-lactoglobulin, whey proteins and protein isolates. Polysaccharides such as gum Arabic and modified starch.	Joye and McClements (2013); Donsì and Ferrari (2016); Bhushani and Anandharamakrishnan (2017)
Protein	Ranges from clear to opaque depending upon their size.	pH and temperature.	Produce larger droplet sizes due to their low absorption kinetics.	Corn protein, zein ultrafine fibers, whey protein and milk protein.	Bhushani and Anandharamakrishnan (2017); Shu et al. (2018)

used in the production of nanoemulsions. Surface active lecithin is extracted from milk, soybeans, rapeseeds, sunflower kernels and egg yolk. Despite possessing the surface-active property, phospholipids are not really good emulsifiers and are prone to coalescence. They are often used in combination with other protein-based emulsifiers.

10.3.2 Surfactant-Based Nanosystems

Non-ionic food-grade surfactants are relatively stable against coalescence and flocculation when compared to protein-based and lipid-based emulsifiers (Silva et al. 2015; Chang and McClements 2016; Ozturk and McClements 2016). Negatively charged ionic surfactants are also used in food grade delivery system. Hydrophilic lipophilic balance (HLB) value contributes significantly during the selection of surfactant in nanoemulsion fabrication (Sugumar et al. 2013; Dizaj et al. 2016). HLB number indicates affinity of surfactant for oil phase or aqueous phase. Small molecule surfactant used in low energy method differs by their HLB number and molecular geometry. Molecular geometry of surfactant influences whether the assembly of droplets will be into either O/W or W/O nanoemulsions. HLB >10 induces formation of O/W nanoemulsion with small droplet size (Ozturk and McClements 2016). Propylene glycol, ethanol and glycerol are co-solvents surfactants which change the properties of aqueous phase and the changes particle size in nanoemulsions (Ozturk and McClements 2016).

10.3.3 Biopolymer-Based Nanosystems

When nanoemulsions are consumed, the biopolymer emulsifiers prevent the flocculation of oil droplets under acidic conditions in stomach (Zou et al. 2015). Amphiphilic proteins and polysaccharides are biopolymers with high molecular weight which act as good emulsifiers (Ozturk and McClements 2016). When two or more biopolymer emulsifiers are combined, the resistance of nanoemulsions toward droplet growth increases (Shu et al. 2018).

10.3.4 Natural Emulsifiers

Natural emulsifiers are currently used due to the demand for "clean-label" products in food market. They exhibit good emulsifying properties, owing to their structure of non-polar proteins being attached to their hydrophilic carbohydrate chains. Some natural surface-active polysaccharides are used as emulsifiers. The most prominent natural emulsifiers available in the market that exhibit surface activity are Casein and Whey proteins, which are derived from bovine milk (de Oca-Ávalos et al. 2017). Gelatins also exhibit surface activity, but cannot be used as an emulsifier as they do not contribute significantly to stabilizing emulsions. Saponin based emulsifiers such as Quillaja Saponin is commonly used to form emulsions with smaller droplets that must be stable at wide range of environmental stresses (Yang and McClements 2013; Chen et al. 2016; Ozturk and McClements 2016).

10.4 In-Product and In-Body Behavior

Nanoemulsion digestion occurs mainly in the small intestine. Pancreatic lipases in small intestine hydrolyze triglyceride or triacylglycerol (TAG) molecules. Exogenous and endogenous surface-active molecules in bioactive compounds after getting hydrolyzed by lipases are solubilized by intestinal fluids (Rao et al. 2013). The formulation and processing of nanoemulsion in food matrix are done based on functional design principles in order to deliver encapsulated compounds to the targeted sites maintaining their functionality in product (*in-product*) and after consumption (*in-body*). *In-product* behavior depends on the dispersion efficiency and compatibility of nanoemulsion with food matrix of encapsulated compounds. Stability of the absorbed encapsulated compounds within complex environment of food matrices is decided by its reactivity with the food matrix as that environment can be in aqueous or lipid phase. Food treatments processing, intense shearing, preservation and storage at high or low temperature affects the property and reactivity of the bioactive compounds. Temperature changes can result in fragmentation of the compounds making them inactive.

In-body behavior is affected by environment changes such as temperature (high temperature during cooking, body temperature), addition of moisture (chewing), pH (oral, gastrointestinal tract), mechanical shear (chewing, grinding and mastication) and enzymes (gastrointestinal tract), which the encapsulated compounds undergoes with the food matrix (Sessa and Donsi 2015). The bioavailability of encapsulated products is affected by breaking or dissolving process of food matrix in order to promote their absorption by GIT into blood streams, epithelial cell absorption transporting them target sites.

To control and regulate in-body and in-product behaviors suitable delivery system must be used. Solidified lipid phase delivery system can be used to promote efficient dispersion; protecting the encapsulated compound during processing, preservation, preparation and also controlling their release during mastication and gastrointestinal digestion; enhancing taste, bio accessibility and bioavailability. Adequate selection of stabilization layer will maintain electrostatic repulsion and steric hindrance between nanoemulsion droplets. Surface composition and charge plays an important role on nanoemulsion's interaction with external environment (Pinheiro et al. 2013; Majeed et al. 2016). Regulating mean particle size, formulation, composition, concentration, number of lipid/polymer layers over of lipophilic core can influence the rate of lipid digestion and its kinetic stability (Donsì et al. 2013).

Lipase concentration present per unit surface area decreases with a decrease in droplet size increasing lipid digestion rate (Salvia-Trujillo et al. 2013; Walker et al. 2015; Majeed et al. 2016). As the concentration of digestible TAG molecules decrease in oil phase, the bioaccessibility of β-carotene-enriched nanoemulsions also decreased (Rao et al. 2013). A contradictory phenomenon to that proposed by Salvia-Trujillo et al. (2013) was reported by Yi et al. (2015) observing an increase in bioavailability by decreasing the particle size of β-carotene. Compared to medium chain triglyceride and non-digestible oil carrier, long chain triglyceride fatty acid oil carriers of β-carotene were found to have higher bioaccesibility (Bhushani and Anandharamakrishnan 2017). Curcumin incorporation within nanoemulsion has increased its oral bioavailability up to nine folds and the anti-inflammatory activity was also increased compared to unformulated curcumin (Dizaj et al. 2016). It was found that the higher the lipid carrier chain length, the higher is the bioaccesibility of curcumin (Salvia-Trujillo et al. 2017). Curcumin sustained release can also be achieved using multilayer nanoemulsions (Sari et al. 2015; Pinheiro et al. 2016).

10.5 Production

The fabrication of nanoemulsion requires an organic phase, aqueous phase, surfactant and energy. The formation of nanoemulsion is not a spontaneous process as either an internal or external energy input is necessary (Karthik et al. 2017). Production approaches of food-grade nanoemulsions are broadly categorized as either 'top-down' or 'bottom-up' approach. Top-down approach of nanoemulsion fabrication involves mechanical size reduction of the nanoemulsions, such as colloid milling and grinding. It is an energy intensive method, which is commonly referred as a high energy method (Donsì and Ferrari 2016; Abdullaeva 2017; Prakash et al. 2018). Bottom-up approach of nanoemulsion fabrication refers to the synthesis of large structures by the controlled assembly of smaller particles such as atoms and molecules (Abdullaeva 2017; McClements 2015). Bottom-up approach requires low energy to produce very fine droplets using low cost equipment. It is thus commonly known as a low energy method (Prakash et al. 2018). These methods applied in the fabrication of nanoemulsion have different emulsion composition and operating conditions, which regulates its droplet size (Table 10.2) (Karthik et al. 2017).

10.5.1 High Energy Methods

Top-down high energy method involves the use of mechanical instruments such as ultra sound generators, high-shear stirrer, and high-pressure homogenizer to produce nanoemulsions by generating powerful disruptive forces (Solans and Solé 2012). Intense energy generates high intensity disruptive forces which can disrupt the oil

Table 10.2 Difference between low energy and high energy production methods

Basis	High energy method	Low energy method	References
Quantity	Less quantity of nanoemulsions is formed.	A relatively large quantity of nanoemulsions is produced.	Jasmina et al. (2017)
Solvent-oil ratio (SOR)	Lower SOR is required to produce small droplets.	Higher SOR is required for the formation of smaller droplets.	Yang et al. (2012); Jasmina et al. (2017)
Energy requirement	Requires sophisticated instruments which takes up large amount of energy.	Involves user-friendly equipment, with low energy in-take. Thus, it is more acceptable in market.	Yang et al. (2012); Jasmina et al. (2017)
Cost	Expensive procedure.	Inexpensive procedure.	Jasmina et al. (2017)
Temperature	Large energy and high temperature promote component degradation.	Temperature remains constant, degradation does not occur.	Jasmina et al. (2017)
Ingredients incorporated	Thermo-labile active ingredients such as proteins and retinoids cannot be incorporated.	Any ingredient can be incorporated.	Yang et al. (2012); Jasmina et al. (2017)
Surfactant	Flexible in the choice of the internal structure and surfactant, as well as possibility of preparing nanoemulsions within a short duration.	Only non-ionic surfactant can be used, mostly all ingredients can be added.	Jasmina et al. (2017)

and water phase forming tiny oil droplets into aqueous phase (Yang et al. 2012; Silva et al. 2015; Walker et al. 2015). The disruptive forces generated are larger than the restoring forces, which helps to maintain the spherical shape of the droplets. In high energy methods, the nanoemulsion droplet size depends on interfacial tension, duration of energy input, energy intensity, relative viscosities of the phases, types of emulsifier, concentration of emulsifiers and surfactant-to-oil ratio (SOR < 0.1) (McClements 2012; Yang et al. 2012; Karthik et al. 2017). Smaller droplet sizes are preferred by the food industry for the fabrication of food-grade nanoemulsions which can be obtained by controlling the viscosity ratio, increasing the homogenization duration, or by increasing the emulsifier concentration (Karthik et al. 2017). The high energy techniques widely used to produce food-grade nanoemulsions are ultrasonication, high pressure valve homogenization and microfluidization (Yang et al. 2012; Abdullaeva 2017).

High pressure valve homogenizer applies the principle of using multiple passes and exceptional high pressure in the fabrication of nanoemulsion with the required droplet size (Lee et al. 2014). The homogenizer generates small droplets through the disintegration of large droplets by amalgamating the disruptive forces such as shear stress, cavitation and turbulent flow. Nanoemulsions enriched with thyme oil, curcumin and β-carotene are produced using high energy method with varying operating conditions (Karthik et al. 2017). Microfluidizer has a similar design, but differs in the flow of emulsion channels. The principle is to divide an emulsion flowing in a channel into two separate streams. Each stream then passes through a distinct channel. These two streams are then directed towards each other in the interaction chamber. Interaction between the two fast-moving streams creates intense disruptive forces in the interaction chamber, which results in droplet distribution (Lee et al. 2014; Komaiko et al. 2015; Ricaurte et al. 2016). In this method, the factors affecting homogenization efficiency are emulsifier concentration, emulsifier type, oil-water viscosity ratio and oil-water interfacial tension. Food-grade nanoemulsions from food ingredients can be produced using this method (Yang et al. 2012; Karthik et al. 2017).

Nanoemulsions enriched with varieties of bioactive compounds are produced through microfluidizer technique (Salvia-Trujillo et al. 2013; Karthik et al. 2017). The flaw of microfluidization is that, in low surfactant concentration sufficient surfactant quantity is not present to envelope the droplet surface, which causes the droplets to come in close proximity resulting in coalescence. High surfactant concentration does not affect droplet size during homogenization (Yang et al. 2012). Ultrasonication principle states that high ultrasonic waves with a frequency greater than 20 kHz can form nano-sized droplets of approximately 70 nm. The droplet size decreases with increase in the emulsifier concentration, sonication time and power level (Karthik et al. 2017). High energy methods can be applied to fabricate nanoemulsions in large scale, however there are several limitations associated with this method. The limitations of high energy methods are the high cost of operation, the high initial equipment required, the high-power requirement, the high probability of equipment break down and the difficulty in producing fine droplets with food ingredients such as highly viscous oils and slowly adsorbing emulsifiers (Yang et al. 2012).

10.5.2 Low Energy Methods

Energy efficient, bottom-up low energy method, utilizes the system's internal chemical energy and simple stirring to produce nanoemulsions with smaller droplets sizes and low polydispersity than high energy methods (Solans and Solé 2012; Karthik et al. 2017). In low energy mode, nanoemulsions are produced due to the chemical energy released from phase transitions which occurs during emulsification process (Karthik et al. 2017). Fabrication of nanoemulsions through low energy method requires internal energy of oil phase, aqueous phase and emulsifier system (Abdullaeva 2017). There is substantial interest in this field as low energy techniques are energy efficient, relatively inexpensive, facile, capable of producing smaller particle size, and prevent encapsulated compound from being degraded. In this method, the spontaneous formation of smaller oil droplet size is dependent upon the system composition (ionic strength, surfactant type and surfactant-oil-water ratio), and the environmental conditions (stirring speed, duration and temperature) (Karthik et al. 2017; Walker et al. 2015). This phenomenon transpires through the alteration of environmental conditions such as temperature and composition (Silva et al. 2015; Karthik et al. 2017). Solans and Solé (2012) classified low energy methods as spontaneous emulsification or self-emulsification (SE) and phase inversion method (Bhushani and Anandharamakrishnan 2017). Emulsion phase inversion (EPI) and SE are the two main isothermal methods involved in the production of food-grade nanoemulsions. Other isothermal method includes emulsion inversion point (EIP), also referred as phase inversion composition (PIC) and direct emulsification inversion (DEI) method. Thermal method requires changes in temperature to fabricate nanoemulsions, thus the main thermal method used is phase inversion temperature (PIT) method (Komaiko and McClements 2016; Karthik et al. 2017). Low energy methods can be applied to produce nanoemulsions incorporated with nutrients, nutraceuticals and vitamins (Komaiko and McClements 2016). Flavored nanoemulsions can also be prepared through this method (Gupta et al. 2016). However, food products with relatively high levels of fat are not formed by low energy methods due to the presence of excess levels of surfactant in product (de Oca-Ávalos et al. 2017).

10.5.2.1 Spontaneous Emulsification

Spontaneous emulsification (SE) is the spontaneous formation of nanoemulsions when aqueous and organic phase are mixed at constant temperature (Yang et al. 2012; Solans and Solé 2012; Komaiko and McClements 2014; Karthik et al. 2017). The organic phase of emulsion is concocted by lipophilic surfactant, water miscible solvent and oil. The aqueous phase is composed of hydrophilic surfactant and water. When both aqueous and organic phases are mixed, a non-equilibrium stage is achieved. At this stage, rapid diffusion of the water miscible solvent occurs without any phase transition between organic and aqueous phase which increases the interfacial area, resulting in a metastable system also the surfactant spontaneous curvature remains unvaried (Bhushani and Anandharamakrishnan 2017). Mercuri et al. (2011) proposed that when a surfactant/oil (S/O) mixture is in contact with the aqueous phase, a boundary initially forms between the S/O and aqueous phase. Water then penetrates the S/O layer causing swelling to occur, which initially results in a W/O microemulsion, then forms liquid crystalline phases. A liquid crystalline fragment crosses the boundary and enters into aqueous phase. Here the fragments further break down to form nano-sized emulsions (Yang et al. 2012). The turbulence caused during solvent diffusion aids in the formation of nanoemulsion (Solans and Solé 2012). The mechanisms having a key role in nanoemulsion fabrication are interfacial turbulence, negative interfacial tension, diffusion, stranding and dispersion (Bhushani and Anandharamakrishnan 2017). SE forms smaller droplet sizes; however, it requires high surfactant concentration when compared to high energy methods. SOR (surfactant-oil-ratio) for microfluidization is SOR < 0.1, whereas SOR for SE is SOR >1 (Yang et al. 2012). Spontaneous formation of nanoemulsions can be carried out by varying the composition of both phases, environmental conditions such as pH, ionic strength and temperature and mixing conditions which includes order of addition, agitation speed and rate of addition.

10.5.2.2 Phase Inversion Method

Phase inversion methods are followed if surfactant spontaneous curvature changes from negative to positive producing O/W nanoemulsions or from positive to negative producing W/O nanoemulsions during emulsification (Solans and Solé 2012). Phase inversion methods are categorized into two: PIT and PIC (Solans and Solé 2012; Walker et al. 2015). Phase transitions occur by changing the composition (PIC) or the temperature (PIT) (Kotta et al. 2013). PIT was pioneered in 1968 by Shinoda. Here the temperature is varied to alter the solubility and optimum curvature of non-ionic surfactants. This converts O/W emulsions into W/O emulsions or vice versa. In this method, the mixture is heated to a temperature higher than the PIT, followed by instant cooling by constant stirring which forms nanoemulsions (Walker et al. 2015). PIT method is applicable only for temperature sensitive surfactants such as polyoxy-ethylene-type nonionic surfactants that undergo hydration in poly (oxyethylene) chain and change its curvature as temperature changes. When the system's lipophilic and hydrophilic properties are balanced, the mean spontaneous curvature of surfactant molecule is zero. In PIC method phase transitions are introduced by changing the composition at a steady temperature during emulsification. This method can be applied to any type of surfactant (Solans and Solé 2012).

Recent methods used to produce nanoemulsions are evaporative ripening and bubble bursting methods at oil/water interface. Bubble bursting method involves the bubbling of gas through an aqueous phase containing surfactant. Once the bubble arrives at the interface, the oil film formed between the water phase and interface drains slowly, and a dimple is created in the water-air interface which generates and nucleates spatters of oil droplets in the water phase. In Evaporative Ripening method, smaller emulsion droplets are prepared using high viscosity oils. The initial droplets produced from HPH are a mixture of non-volatile (high molecular weight) and volatile (low molecular weight) oils. During heating, the volatile components present in the droplets evaporate causing the droplets to shrink and thus allows the formation of rich oil phase in the high molecular weight oil (Gupta et al. 2016).

10.6 Applications of Nanoemulsions

Nanotechnology has found ways for its application in the food industry by using nanoparticles in packaging and active/intelligent packaging. The latter can extend the shelf-life of the food, as well as maintaining the quality and safety of them (Bracone et al. 2016). The components involved here are indicators such as antioxidants, mineral oils, sugars, methylene blue and nanosensors for contamination detection (Abdullaeva 2017). Nanoemulsions are used to design smart foods with ingredients that are usually difficult to incorporate due to low water stability improving nanodelivery of nutrients (Gupta et al. 2016). Their various other applications in the food industry includes protection, encapsulation and delivery of food bioactives, nutrients, vitamins and controlled release of flavors and incorporation of antimicrobial and anti-oxidant compounds (Bhushani and Anandharamakrishnan 2017).

Catechins, nonpolar components such as triacylglycerol (corn, soybean, algae, fish oil), free fatty acids, mineral oils, waxes, acids are some of the compounds when encapsulated in nanoemulsions possess properties such as high stability, high retention time, improved solubility and increased absorption due to their direct absorption from gastro intestinal tract (Dizaj et al. 2016; Bhushani and Anandharamakrishnan 2017; Gadkari et al. 2017). Work has been done by several scientists in development of soya protein based nanoemulsion with improved chemical stability and bioaccessibility, docasahexaenoic acid nanoemulsion with improved physical and chemical stability and monolayer permeability of Caco-2 cells of green tea catechins (Bhushani et al. 2016; Karthik and Anandharamakrishnan 2016).

Nanoemulsions can fortify foods, such as milk cereal products or bread and can also be incorporated into beverages (Öztürk 2017). These are also used as nutraceuticals (quercetin, vitamins as D3 carotenoids) and food supplements (Bhushani and Anandharamakrishnan 2017). For a modest preservative in food industry especially for minimally processed fruits and vegetables (MPFV) essential oils are used. Due to their small size and presence of emulsifiers it gets easily transported through porin proteins of the outer membrane in gram negative bacteria, causing the leakage of cytoplasmic constituents which in turn results in cell viability (Donsì and Ferrari 2016). Some of the other applications of nanoemulsion in food industries are shown in Table 10.3.

10.7 Limitations

Nanoemulsions have great benefits over conventional emulsions, especially in the food and beverage industry. But along with its advantages it has some challenges such as the risks associated with its intake, digestion and potential toxicity to the human body (McClements 2013). There are apprehensions regarding the toxicity associated with its applications in food. Some concerns were raised regarding the incorporation of nanoparticles into foods including the delivery systems for colors, flavors, preservatives, nutraceuticals and those used to alter the properties of food or food packaging. The prospective toxicity mechanisms of different food grade nanoparticles include physiological and physiochemical mechanisms. Most of them may not have adverse effects on human health but some could have. There has been a considerable increase in the study of the potential toxic effects of food-grade nanoparticles in the past few years. These studies concluded that food grade nanoparticles may have unfavorable effects on health. But there is still some uncertainty in this area (McClements and Xiao 2017).

ADME (absorption, distribution, metabolism, excretion) is also affected in a negative way due to the potential toxicity of nanoemulsions (McClements 2013). Due to small size of nanoemulsions, their behavior within the human body may differ from conventionally utilized larger particles or bulk materials ingredients. Depending on the nature of the nanoemulsions and the properties of the food matrix they are dispersed. The safety of nanoemulsions should be judged on a case-by-case basis (McClements and Xiao 2017). To test the toxicity under reproducible and

Table 10.3 Bioactive compounds with their benefits when encapsulated in nanoemulsions and limitations as unformulated compounds

Bioactives used	Usefulness of nanoemulsion	Benefits of bioactive compound added to food	Limitations overcame	References
Omega-3 fatty acids	Increased water-dispersibility, stability, absorption and oral bioavailability, mask undesirable off-flavors	Improves brain development, reduces the risk of cardiovascular disease, mental disorders as well as diseases related to immune response disorders.	Susceptible to chemical degradation in visible or ultraviolet radiation, poor oxidative stability, low water solubility and variable bioavailability	Walker et al. (2015); Dizaj et al. (2016); Bush et al. (2017)
Carotenoids(β-carotenoid)	Improved bioavailability and bioaccessibility, improves solubility, stability, digestibility and controlled release.	Used as natural colorant, act as scavengers of active oxygen species, exhibit anti-oxidative effect, reduces risk of heart disease, cancer and macular degeneration.	Low bioavailability, very low water solubility, poor thermal and photo stability.	Rao et al. (2013); Salvia-Trujillo et al. (2013); McClements et al. (2017); Sotomayor-Gerding et al. (2016); Dizaj et al. (2016)
Essential oils	Exhibit physicochemical stability, higher bioaccessibility, absorption, improved antimicrobial activity, increased hepatoprotective property, minimized incorporation impact and reduced organoleptic characteristics.	Exhibit strong anti-bacterial, antiviral, and antifungal activities, decreased compound dosage and increased homogeneity, reduced interaction with other matrix compounds and increased compound stability under stress.	Highly volatile, susceptible to environmental conditions, have strong organoleptic characteristics, low stability, poor water solubility and fast oxidation.	Odriozola-Serrano et al. (2014); Severino et al. (2014); Donsì et al. (2014); Mostafa et al. (2015); Donsì and Ferrari (2016); Dizaj et al. (2016); Bhushani and Anandharamakrishnan (2017)
Phytosterols	Improves the solubility, intestinal absorption and bioavailability.	Act as anti-cholesterol agents.	Low solubility in both water and fat that causes their poor absorption.	Dizaj et al. (2016)
Coenzyme Q 10	Improve digestion, solubility and oral bioavailability.	Exhibit bioenergetic, antioxidant, anti-antherogenic effect, inhibits protein and DNA oxidation.	Insoluble in both water and fat.	Littarru and Tiano (2007); Cho et al. (2014); Bhushani and Anandharamakrishnan (2017)
Oil soluble vitamins (vitamins A, D, E and K)	Improve bioavailability, increased transparency, thermal and storage stability.	Used as a health supplement in the beverage industry, exhibit antioxidant, anti-inflammatory, anti-cholesterol and antimicrobial activity thus increases the shelf life of fruit juice.	Water insoluble and thermally unstable.	Hategekimana et al. (2015); Dasgupta et al. (2016); Öztürk (2017); Bhushani and Anandharamakrishnan (2017)

(continued)

Table 10.3 (continued)

Bioactives used	Usefulness of nanoemulsion	Benefits of bioactive compound added to food	Limitations overcame	References
Resveratrol	Increased stability in alkaline medium and on exposure to UV up to 88%, control release rate which aids in targeted delivery and improved transport through cell monolayer.	Antioxidant, anti-inflammatory, suppresses cancer and heart disease.	Susceptible to chemical degradation under exposure to visible light or ultraviolet radiation, instable in water and chemicals resulting in its poor bioavailability.	Joye et al. (2014); McClements (2015); Davidov-Pardo and McClements (2014); Bhushani and Anandharamakrishnan (2017)
Curcumin	Ease digestion process, increase permeation; bioaccessibility and physiochemical stability at high temperature, pH and varying ionic strength.	Exhibit anti-inflammatory, antioxidant, anticancer and antimicrobial activity.	Susceptible to chemical degradation upon exposure to visible light and ultraviolet radiation.	Li et al. (2015); Sari et al. (2015); Salvia-Trujillo et al. (2016) Pinheiro et al. (2016); Bhushani and Anandharamakrishnan (2017)
Bovine lactoferrin	Prevent its denaturation from proteolysis and dilution effects, retained its biological activity and 3D structure, inhibit the iron absorption of pathogenic bacteria.	Have anti-inflammatory, anti-oxidant, anti-viral, anti-bacterial, anti-fungal effect against pathogenic bacteria and candida albicans and mediates immunomodulatory activities.	Being a protein can be denature on high temperature, pH changes in GIT.	Balcão et al. (2013)
Quercetin	Bioaccessibility increased two-folds.	Shows antioxidant, anti-inflammatory, anti-diabetic and anti-hyperlipidemic effect, and reduce risk of cardiovascular disease, metabolic disorder, and certain types of cancer.		Joye et al. (2014); Aditya et al. (2014); David et al. (2016)
Flavors (D-limonene)	Used in baked foods and beverages, proven to improve physical and temperature stability (at 25 °C).	Act as food flavorants, exhibit antioxidant, antimicrobial and poses therapeutic properties.	Poor chemical stability to light, presence of oxidants and temperature, wherein at high temperature it forms isoprene molecules which is prone to oxidation.	Zahi et al. (2015); Li and Lu (2016); Dizaj et al. (2016); Abdullaeva (2017); Bhushani and Anandharamakrishnan (2017)

realistic conditions, there is need to standardize and develop systematic methods (McClements and Xiao 2017).

Scarcity of natural food compatible emulsifiers limits its use in large scale industry. Also, the capital cost of homogenization system required for high-throughput is typically high for food industry. Regulatory bodies have concerns about the acceptance of nanotechnology in foods as there are hardly any predictable interactions available till date between nanoemulsions and its complex food system. All these reasons limit the use of nanoemulsions as bioactive compounds delivery through food (Donsì 2018).

10.8 Conclusion and Future Aspects

Nanoemulsions with a droplet size of 20–1000 nm are used for the controlled and targeted release of lipophilic, amphiphilic and hydrophilic bioactive compounds, and nutraceuticals, as they are chemically unstable. The O/W nanoemulsions can effectively deliver bioactive compounds, antimicrobial agents, dyes, flavors, etc., and at the same time maintain and improve their chemical stability, thus increasing the bioavailability of the loaded substances. These compounds improve the nutritional content, the aroma, the shelf life, the pharmacokinetics of foods and control the release, digestion and absorption of products encapsulated in the gastrointestinal tract, making the healthier food product. Due to its potential advantage over conventional emulsions, it is receiving great attention from the food industry, although they are still not widely used today. The emulsifying properties using natural surfactants (sugar esters and lecithin), lipids and biopolymers (vegetable and animal proteins, modified starch and natural gums) are improved using nanometric emulsion methods. Nanoemulsions can also impart functional properties through the encapsulation of active substances, which can be benefits on the food quality and safety. A reduction in equipment costs and the development of new production methods for nanoemulsions will give rise to a greater boom. Since in the future functional, healthy and medicinal foods will be increasingly demanded by society, nanoemulsion systems being applied to active food ingredients will be a valuable tool.

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References

Abdullaeva, Z. (2017). Nanomaterials in food industry and packaging. In *Nanomaterials in daily life* (pp. 23–46). Cham: Springer. https://doi.org/10.1007/978-3-319-57216-1_2.

Aditya, N. P., Macedo, A. S., Doktorovova, S., Souto, E. B., Kim, S., Chang, P. S., & Ko, S. (2014). Development and evaluation of lipid nanocarriers for quercetin delivery: A comparative study of solid lipid nanoparticles (SLN), nanostructured lipid carriers (NLC), and lipid nanoemulsions (LNE). *LWT-Food Science and Technology, 59*(1), 115–121. https://doi.org/10.1016/j.lwt.2014.04.058.

Balcão, V. M., Costa, C. I., Matos, C. M., Moutinho, C. G., Amorim, M., Pintado, M. E., Gomes, A. P., Vila, M. M., & Teixeira, J. A. (2013). Nanoencapsulation of bovine lactoferrin for food and biopharmaceutical applications. *Food Hydrocolloids, 32*(2), 425–431. https://doi.org/10.1016/j.foodhyd.2013.02.004.

Bhushani, A., & Anandharamakrishnan, C. (2017). Food-grade nanoemulsions for protection and delivery of nutrients. In *Nanoscience in food and agriculture* (Vol. 4, pp. 99–139). Cham: Springer. https://doi.org/10.1007/978-3-319-53112-0_3.

Bhushani, J. A., Karthik, P., & Anandharamakrishnan, C. (2016). Nanoemulsion based delivery system for improved bioaccessibility and Caco-2 cell monolayer permeability of green tea catechins. *Food Hydrocolloids, 56*, 372–382. https://doi.org/10.1016/j.foodhyd.2015.12.035.

Bracone, M., Merino, D., González, J., Alvarez, V. A., & Gutiérrez, T. J. (2016). Chapter 6. Nanopackaging from natural fillers and biopolymers for the development of active and intelligent films. In S. Ikram & S. Ahmed (Eds.), *Natural polymers: Derivatives, blends and composites* (pp. 119–155). New York. EE.UU. ISBN: 978-1-63485-831-1: Editorial Nova Science Publishers, Inc.

Bush, L., Stevenson, L., & Lane, K. E. (2017). The oxidative stability of omega-3 oil-in-water nanoemulsion systems suitable for functional food enrichment: A systematic review of the literature. *Critical Reviews in Food Science and Nutrition*, 1–15. https://doi.org/10.1080/10408398.2017.1394268.

Chang, Y., & McClements, D. J. (2016). Influence of emulsifier type on the in vitro digestion of fish oil-in-water emulsions in the presence of an anionic marine polysaccharide (fucoidan): Caseinate, whey protein, lecithin, or Tween 80. *Food Hydrocolloids, 61*, 92–101. https://doi.org/10.1016/j.foodhyd.2016.04.047.

Chellaram, C., Murugaboopathi, G., John, A. A., Sivakumar, R., Ganesan, S., Krithika, S., & Priya, G. (2014). Significance of nanotechnology in food industry. *APCBEE Procedia, 8*, 109–113. https://doi.org/10.1016/j.apcbee.2014.03.010.

Chen, X. W., Chen, Y. J., Wang, J. M., Guo, J., Yin, S. W., & Yang, X. Q. (2016). Phytosterol structured algae oil nanoemulsions and powders: Improving antioxidant and flavor properties. *Food and Function, 7*(9), 3694–3702. https://doi.org/10.1039/c6fo00449k.

Cho, H. T., Salvia-Trujillo, L., Kim, J., Park, Y., Xiao, H., & McClements, D. J. (2014). Droplet size and composition of nutraceutical nanoemulsions influences bioavailability of long chain fatty acids and coenzyme Q10. *Food Chemistry, 156*, 117–122. https://doi.org/10.1016/j.foodchem.2014.01.084.

Dasgupta, N., Ranjan, S., Mundra, S., Ramalingam, C., & Kumar, A. (2016). Fabrication of food grade vitamin E nanoemulsion by low energy approach, characterization and its application. *International Journal of Food Properties, 19*(3), 700–708. https://doi.org/10.1080/10942912.2015.1042587.

David, A. V. A., Arulmoli, R., & Parasuraman, S. (2016). Overviews of biological importance of quercetin: A bioactive flavonoid. *Pharmacognosy Reviews, 10*(20), 84–89. https://doi.org/10.4103/0973-7847.194044.

Davidov-Pardo, G., & McClements, D. J. (2014). Resveratrol encapsulation: Designing delivery systems to overcome solubility, stability and bioavailability issues. *Trends in Food Science and Technology, 38*(2), 88–103. https://doi.org/10.1016/j.tifs.2014.05.003.

de Oca-Ávalos, J. M. M., Candal, R. J., & Herrera, M. L. (2017). Nanoemulsions: Stability and physical properties. *Current Opinion in Food Science, 16*, 1–6. https://doi.org/10.1016/j.cofs.2017.06.003.

Dizaj, S. M., Yaqoubi, S., Adibkia, K., & Lotfipour, F. (2016). Nanoemulsion-based delivery systems: Preparation and application in the food industry. In *Emulsions* (pp. 293–328). https://doi.org/10.1016/b978-0-12-804306-6.00009-x.

Donsì, F. (2018). Applications of Nanoemulsions in foods. In *Nanoemulsions* (pp. 349–377). https://doi.org/10.1016/b978-0-12-811838-2.00011-4.

Donsì, F., & Ferrari, G. (2016). Essential oil nanoemulsions as antimicrobial agents in food. *Journal of Biotechnology, 233*, 106–120. https://doi.org/10.1016/j.jbiotec.2016.07.005.

Donsì, F., Sessa, M., & Ferrari, G. (2013). Nanometric-size delivery Systems for Bioactive Compounds for the nutraceutical and food industries. In *Bio-nanotechnology: A revolution in food, biomedical and health sciences* (pp. 619–666). https://doi.org/10.1002/9781118451915.ch37.

Donsì, F., Cuomo, A., Marchese, E., & Ferrari, G. (2014). Infusion of essential oils for food stabilization: Unraveling the role of nanoemulsion-based delivery systems on mass transfer and antimicrobial activity. *Innovative Food Science and Emerging Technologies, 22*, 212–220. https://doi.org/10.1016/j.ifset.2014.01.008.

Gadkari, P. V., Shashidhar, M. G., & Balaraman, M. (2017). Delivery of green tea catechins through oil-in-water (O/W) nanoemulsion and assessment of storage stability. *Journal of Food Engineering, 199*, 65–76. https://doi.org/10.1016/j.jfoodeng.2016.12.009.

Gupta, A., Eral, H. B., Hatton, T. A., & Doyle, P. S. (2016). Nanoemulsions: Formation, properties and applications. *Soft Matter, 12*(11), 2826–2841. https://doi.org/10.1039/c5sm02958a.

Gutiérrez, T. J. (2018a). Are modified pumpkin flour/plum flour nanocomposite films biodegradable and compostable? *Food Hydrocolloids, 83*, 397–410. https://doi.org/10.1016/j.foodhyd.2018.05.035.

Gutiérrez, T. J. (2018b). Chapter 55. Processing nano- and microcapsules for industrial applications. In C. M. Hussain (Ed.). Editorial Elsevier. EE.UU. ISBN: 978–0–12-813351-4. *Handbook of nanomaterials for industrial applications* (pp. 989–1011). https://doi.org/10.1016/B978-0-12-813351-4.00057-2.

Gutiérrez, T. J., & Álvarez, K. (2017). Chapter 6. Biopolymers as microencapsulation materials in the food industry. In M. Masuelli & D. Renard (Eds.), *Advances in physicochemical properties of biopolymers: Part 2* (pp. 296–322). Bentham Science Publishers. EE.UU. ISBN: 978–1–68108-545-6. eISBN: 978–1–68108-544-9,. https://doi.org/10.2174/9781681085449117010009.

Gutiérrez, T. J., & Alvarez, V. A. (2018). Bionanocomposite films developed from corn starch and natural and modified nano-clays with or without added blueberry extract. *Food Hydrocolloids, 77*, 407–420. https://doi.org/10.1016/j.foodhyd.2017.10.017.

Gutiérrez, T. J., Ponce, A. G., & Alvarez, V. A. (2017). Nano-clays from natural and modified montmorillonite with and without added blueberry extract for active and intelligent food nanopackaging materials. *Materials Chemistry and Physics, 194*, 283–292. https://doi.org/10.1016/j.matchemphys.2017.03.052.

Gutiérrez, T. J., Toro-Márquez, L. A., Merino, D., & Mendieta, J. R. (2019). Hydrogen-bonding interactions and compostability of bionanocomposite films prepared from corn starch and nano-fillers with and without added Jamaica flower extract. *Food Hydrocolloids, 89*, 283–293. https://doi.org/10.1016/j.foodhyd.2018.10.058.

Guttoff, M., Saberi, A. H., & McClements, D. J. (2015). Formation of vitamin D nanoemulsion-based delivery systems by spontaneous emulsification: Factors affecting particle size and stability. *Food Chemistry, 171*, 117–122. https://doi.org/10.1016/j.foodchem.2014.08.087.

Hategekimana, J., Chamba, M. V., Shoemaker, C. F., Majeed, H., & Zhong, F. (2015). Vitamin E nanoemulsions by emulsion phase inversion: Effect of environmental stress and long-term storage on stability and degradation in different carrier oil types. *Colloids and Surfaces A: Physicochemical and Engineering Aspects, 483*, 70–80. https://doi.org/10.1016/j.colsurfa.2015.03.020.

Helgeson, M. E. (2016). Colloidal behavior of nanoemulsions: Interactions, structure, and rheology. *Current Opinion in Colloid and Interface Science, 25*, 39–50. https://doi.org/10.1016/j.cocis.2016.06.006.

Homs, M., Calderó, G., Monge, M., Morales, D., & Solans, C. (2018). Influence of polymer concentration on the properties of nano-emulsions and nanoparticles obtained by a low-energy method. *Colloids and Surfaces A: Physicochemical and Engineering Aspects, 536*, 204–212. https://doi.org/10.1016/j.colsurfa.2017.06.009.

Jasmina, H., Džana, O., Alisa, E., Edina, V., & Ognjenka, R. (2017). Preparation of nanoemulsions by high-energy and lowenergy emulsification methods. In *cmbebih* (pp. 317–322). Singapore: Springer. https://doi.org/10.1007/978-981-10-4166-2_48.

Joye, I. J., & McClements, D. J. (2013). Production of nanoparticles by anti-solvent precipitation for use in food systems. *Trends in Food Science & Technology, 34*(2), 109–123. https://doi.org/10.1016/j.tifs.2013.10.002.

Joye, I. J., Davidov-Pardo, G., & McClements, D. J. (2014). Nanotechnology for increased micronutrient bioavailability. *Trends in Food Science and Technology, 40*(2), 168–182. https://doi.org/10.1016/j.tifs.2014.08.006.

Karthik, P., & Anandharamakrishnan, C. (2016). Fabrication of a nutrient delivery system of docosahexaenoic acid nanoemulsions via high energy techniques. *RSC Advances, 6*(5), 3501–3513. https://doi.org/10.1039/C5RA12876E.

Karthik, P., Ezhilarasi, P. N., & Anandharamakrishnan, C. (2017). Challenges associated in stability of food grade nanoemulsions. *Critical Reviews in Food Science and Nutrition, 57*(7), 1435–1450. https://doi.org/10.1080/10408398.2015.1006767.

Komaiko, J., & McClements, D. J. (2014). Optimization of isothermal low-energy nanoemulsion formation: Hydrocarbon oil, non-ionic surfactant, and water systems. *Journal of Colloid and Interface Science, 425*, 59–66. https://doi.org/10.1016/j.jcis.2014.03.035.

Komaiko, J. S., & McClements, D. J. (2016). Formation of food-grade nanoemulsions using low-energy preparation methods: A review of available methods. *Comprehensive Reviews in Food Science and Food Safety, 15*(2), 331–352. https://doi.org/10.1111/1541-4337.12189.

Komaiko, J., Sastrosubroto, A., & McClements, D. J. (2015). Formation of oil-in-water emulsions from natural emulsifiers using spontaneous emulsification: Sunflower phospholipids. *Journal of Agricultural and Food Chemistry, 63*(45), 10078–10088. https://doi.org/10.1021/acs.jafc.5b03824.

Kotta, S., Khan, A. W., Ansari, S. H., Sharma, R. K., & Ali, J. (2013). Formulation of nanoemulsion: A comparison between phase inversion composition method and high-pressure homogenization method. *Drug Delivery, 22*(4), 455–466. https://doi.org/10.3109/10717544.2013.866992.

Lee, L., Hancocks, R., Noble, I., & Norton, I. T. (2014). Production of water-in-oil nanoemulsions using high pressure homogenisation: A study on droplet break-up. *Journal of Food Engineering, 131*, 33–37. https://doi.org/10.1016/j.jfoodeng.2014.01.024.

Li, P. H., & Lu, W. C. (2016). Effects of storage conditions on the physical stability of d-limonene nanoemulsion. *Food Hydrocolloids, 53*, 218–224. https://doi.org/10.1016/j.foodhyd.2015.01.031.

Li, M., Cui, J., Ngadi, M. O., & Ma, Y. (2015). Absorption mechanism of whey-protein-delivered curcumin using Caco-2 cell monolayers. *Food Chemistry, 180*, 48–54. https://doi.org/10.1016/j.foodchem.2015.01.132.

Littarru, G. P., & Tiano, L. (2007). Bioenergetic and antioxidant properties of coenzyme Q 10: Recent developments. *Molecular Biotechnology, 37*(1), 31–37. https://doi.org/10.1007/s12033-007-0052-y.

Lorenzo, G., Zaritzky, N., & Califano, A. (2018). Food gel emulsions: Structural characteristics and viscoelastic behavior. In T. J. Gutiérrez (Ed.), *Polymers for food applications* (pp. 481–507). Cham: Springer. https://doi.org/10.1007/978-3-319-94625-2_18.

Majeed, H., Antoniou, J., Hategekimana, J., Sharif, H. R., Haider, J., Liu, F., Ali, B., Liang Rong, L., Ma, J., & Zhong, F. (2016). Influence of carrier oil type, particle size on in vitro lipid digestion and eugenol release in emulsion and nanoemulsions. *Food Hydrocolloids, 52*, 415–422. https://doi.org/10.1016/j.foodhyd.2015.07.009.

McClements, D. J. (2012). Advances in fabrication of emulsions with enhanced functionality using structural design principles. *Current Opinion in Colloid and Interface Science, 17*(5), 235–245. https://doi.org/10.1016/j.cocis.2012.06.002.

McClements, D. J. (2013). Edible lipid nanoparticles: Digestion, absorption, and potential toxicity. *Progress in Lipid Research, 52*(4), 409–423. https://doi.org/10.1016/j.plipres.2013.04.008.

McClements, D. J. (2015). Nanoscale nutrient delivery systems for food applications: Improving bioactive dispersibility, stability, and bioavailability. *Journal of Food Science, 80*(7), N1602–N1611. https://doi.org/10.1111/1750-3841.12919.

McClements, D. J., & Xiao, H. (2017). Is nano safe in foods? Establishing the factors impacting the gastrointestinal fate and toxicity of organic and inorganic food-grade nanoparticles. *npj Science of Food, 1*(1), 6. https://doi.org/10.1038/s41538-017-0005-1.

Merino, D., Gutiérrez, T. J., Mansilla, A. Y., Casalongué, C., & Alvarez, V. A. (2018). Critical evaluation of starch-based antibacterial nanocomposites as agricultural mulch films: Study on their interactions with water and light. *ACS Sustainable Chemistry & Engineering, 6*(11), 15662–15672. https://doi.org/10.1021/acssuschemeng.8b04162.

Mercuri, A., Passalacqua, A., Wickham, M. S., Faulks, R. M., Craig, D. Q., & Barker, S. A. (2011). The effect of composition and gastric conditions on the self-emulsification process of ibuprofen-loaded self-emulsifying drug delivery systems: A microscopic and dynamic gastric model study. Pharmaceutical Research, 28(7), 1540-1551. https://doi.org/10.1007/s11095-011-0387-8

Merino, D., Gutiérrez, T. J., & Alvarez, V. A. (2019). Structural and thermal properties of agricultural mulch films based on native and oxidized corn starch nanocomposites. *Starch-Stärke*. *71*(7–8), 1800341. https://doi.org/10.1002/star.201800341.

Mostafa, D. M., Kassem, A. A., Asfour, M. H., Al Okbi, S. Y., Mohamed, D. A., & Hamed, T. E. S. (2015). Transdermal cumin essential oil nanoemulsions with potent antioxidant and hepatoprotective activities: *in-vitro* and *in-vivo* evaluation. *Journal of Molecular Liquids, 212*, 6–15. https://doi.org/10.1016/j.molliq.2015.08.047.

Odriozola-Serrano, I., Oms-Oliu, G., & Martín-Belloso, O. (2014). Nanoemulsion-based delivery systems to improve functionality of lipophilic components. *Frontiers in Nutrition, 1*, 24. https://doi.org/10.3389/fnut.2014.00024.

Öztürk, B. (2017). Nanoemulsions for food fortification with lipophilic vitamins: Production challenges, stability, and bioavailability. *European Journal of Lipid Science and Technology, 119*(7), 1500539. https://doi.org/10.1002/ejlt.201500539.

Ozturk, B., & McClements, D. J. (2016). Progress in natural emulsifiers for utilization in food emulsions. *Current Opinion in Food Science, 7*, 1–6. https://doi.org/10.1016/j.cofs.2015.07.008.

Pinheiro, A. C., Lad, M., Silva, H. D., Coimbra, M. A., Boland, M., & Vicente, A. A. (2013). Unravelling the behaviour of curcumin nanoemulsions during *in vitro* digestion: Effect of the surface charge. *Soft Matter, 9*(11), 3147–3154. https://doi.org/10.1039/c3sm27527b.

Pinheiro, A. C., Coimbra, M. A., & Vicente, A. A. (2016). *In vitro* behaviour of curcumin nanoemulsions stabilized by biopolymer emulsifiers–effect of interfacial composition. *Food Hydrocolloids, 52*, 460–467. https://doi.org/10.1016/j.foodhyd.2015.07.025.

Prakash, A., Baskaran, R., Paramasivam, N., & Vadivel, V. (2018). Essential oil based nanoemulsions to improve the microbial quality of minimally processed fruits and vegetables: A review. *Food Research International, 111*, 509–523. https://doi.org/10.1016/j.foodres.2018.05.066.

Rao, J., Decker, E. A., Xiao, H., & McClements, D. J. (2013). Nutraceutical nanoemulsions: Influence of carrier oil composition (digestible versus indigestible oil) on β-carotene bioavailability. *Journal of the Science of Food and Agriculture, 93*(13), 3175–3183. https://doi.org/10.1002/jsfa.6215.

Ricaurte, L., de Jesús Perea-Flores, M., Martinez, A., & Quintanilla-Carvajal, M. X. (2016). Production of high-oleic palm oil nanoemulsions by high-shear homogenization (microfluidization). *Innovative Food Science and Emerging Technologies, 35*, 75–85. https://doi.org/10.1016/j.ifset.2016.04.004.

Salvia-Trujillo, L., Qian, C., Martín-Belloso, O., & McClements, D. J. (2013). Influence of particle size on lipid digestion and β-carotene bioaccessibility in emulsions and nanoemulsions. *Food Chemistry, 141*(2), 1472–1480. https://doi.org/10.1016/j.foodchem.2013.03.050.

Salvia-Trujillo, L., Martín-Belloso, O., & McClements, D. J. (2016). Excipient nanoemulsions for improving oral bioavailability of bioactives. *Nanomaterials, 6*(1), 17. https://doi.org/10.3390/nano6010017.

Salvia-Trujillo, L., Soliva-Fortuny, R., Rojas-Graü, M. A., McClements, D. J., & Martín-Belloso, O. (2017). Edible nanoemulsions as carriers of active ingredients: A review. *Annual Review of Food Science and Technology, 8*, 439–466. https://doi.org/10.1146/annurev-food-030216-025908.

Sari, T. P., Mann, B., Kumar, R., Singh, R. R. B., Sharma, R., Bhardwaj, M., & Athira, S. (2015). Preparation and characterization of nanoemulsion encapsulating curcumin. *Food Hydrocolloids, 43*, 540–546. https://doi.org/10.1016/j.foodhyd.2014.07.011.

Sessa, M., & Donsì, F. (2015). Nanoemulsion-based delivery systems. In *Microencapsulation and microspheres for food applications* (pp. 79–94). https://doi.org/10.1016/b978-0-12-800350-3.00007-8.

Severino, R., Vu, K. D., Donsì, F., Salmieri, S., Ferrari, G., & Lacroix, M. (2014). Antibacterial and physical effects of modified chitosan based-coating containing nanoemulsion of mandarin essential oil and three non-thermal treatments against Listeria innocua in green beans. *International Journal of Food Microbiology, 191*, 82–88. https://doi.org/10.1016/j.ijfoodmicro.2014.09.007.

Shariffa, Y. N., Tan, T. B., Abas, F., Mirhosseini, H., Nehdi, I. A., & Tan, C. P. (2016). Producing a lycopene nanodispersion: The effects of emulsifiers. *Food and Bioproducts Processing, 98*, 210–216. https://doi.org/10.1016/j.fbp.2016.01.014.

Shu, G., Khalid, N., Tan, T. B., Zhao, Y., Neves, M. A., Kobayashi, I., & Nakajima, M. (2018). *In vitro* bioaccessibility of ergocalciferol in nanoemulsion-based delivery system: The influence of food-grade emulsifiers with different stabilising mechanisms. *International Journal of Food Science and Technology, 53*(2), 430–440. https://doi.org/10.1111/ijfs.13601.

Silva, H. D., Cerqueira, M. A., & Vicente, A. A. (2015). Influence of surfactant and processing conditions in the stability of oil-in-water nanoemulsions. *Journal of Food Engineering, 167*, 89–98. https://doi.org/10.1016/j.jfoodeng.2015.07.037.

Solans, C., & Solé, I. (2012). Nano-emulsions: Formation by low-energy methods. *Current Opinion in Colloid and Interface Science, 17*(5), 246–254. https://doi.org/10.1016/j.cocis.2012.07.003.

Sotomayor-Gerding, D., Oomah, B. D., Acevedo, F., Morales, E., Bustamante, M., Shene, C., & Rubilar, M. (2016). High carotenoid bioaccessibility through linseed oil nanoemulsions with enhanced physical and oxidative stability. *Food Chemistry, 199*, 463–470. https://doi.org/10.1016/j.foodchem.2015.12.004.

Sugumar, S., Nirmala, J., Ghosh, V., Anjali, H., Mukherjee, A., & Chandrasekaran, N. (2013). Bio-based nanoemulsion formulation, characterization and antibacterial activity against food-borne pathogens. *Journal of Basic Microbiology, 53*(8), 677–685. https://doi.org/10.1002/jobm.201200060.

Toro-Márquez, L. A., Merino, D., & Gutiérrez, T. J. (2018). Bionanocomposite films prepared from corn starch with and without nanopackaged Jamaica (*Hibiscus sabdariffa*) flower extract. *Food and Bioprocess Technology, 11*(11), 1955–1973. https://doi.org/10.1007/s11947-018-2160-z.

Walia, N., Dasgupta, N., Ranjan, S., Chen, L., & Ramalingam, C. (2017). Fish oil based vitamin D nanoencapsulation by ultrasonication and bioaccessibility analysis in simulated gastro-intestinal tract. *Ultrasonics Sonochemistry, 39*, 623–635. https://doi.org/10.1016/j.ultsonch.2017.05.021.

Walker, R., Decker, E. A., & McClements, D. J. (2015). Development of food-grade nanoemulsions and emulsions for delivery of omega-3 fatty acids: Opportunities and obstacles in the food industry. *Food and Function, 6*(1), 41–54. https://doi.org/10.1039/c4fo00723a.

Yang, Y., & McClements, D. J. (2013). Vitamin E bioaccessibility: Influence of carrier oil type on digestion and release of emulsified α-tocopherol acetate. *Food Chemistry, 141*(1), 473–481. https://doi.org/10.1016/j.foodchem.2013.03.033.

Yang, Y., Marshall-Breton, C., Leser, M. E., Sher, A. A., & McClements, D. J. (2012). Fabrication of ultrafine edible emulsions: Comparison of high-energy and low-energy homogenization methods. *Food Hydrocolloids, 29*(2), 398–406. https://doi.org/10.1016/j.foodhyd.2012.04.009.

Yi, J., Lam, T. I., Yokoyama, W., Cheng, L. W., & Zhong, F. (2015). Beta-carotene encapsulated in food protein nanoparticles reduces peroxyl radical oxidation in Caco-2 cells. *Food Hydrocolloids, 43*, 31–40. https://doi.org/10.1016/j.foodhyd.2014.04.028.

Zahi, M. R., Liang, H., & Yuan, Q. (2015). Improving the antimicrobial activity of d-limonene using a novel organogel-based nanoemulsion. *Food Control, 50*, 554–559. https://doi.org/10.1016/j.foodcont.2014.10.001.