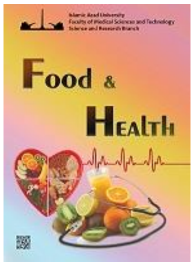
Food & Health 2019, 2(2): 26-31



Food & Health
Journal homepage: fh.srbiau.ac.ir
Journal

Food-grade nanoemulsions and their fabrication methods to increase shelf life

Mina Nasiri [1], Anousheh Sharifan [1], Hamed Ahari [1*], Amir Ali Anvar [2], Shapour Kakoolaki [3]

[1] Department of Food Science and Technology, Science and Research Branch, Islamic Azad University, Tehran, Iran
[2] Department of Food Hygiene, Islamic Azad University, Science and Research Branch, Tehran, Iran
[3] Department of Aquatic Animal Health, Iranian Fisheries Research Organization, Tehran, Iran

ARTICLE INFO

Review Article

Article history:
Received 05 September 2019
Revised 28 October 2019
Accepted 02 December 2019
Available online 15 December 2019

Keywords:
Food-grade nanoemulsions
High-energy production methods
Low-energy production methods

ABSTRACT

In recent years, there has been an increasing interest in the utilization of emulsion and food-grade nanoemulsions and their fabrication methods, and methods have evolved in the food industry and other fields. Emulsions, according to droplet diameter and stability, are divided into three important groups of conventional emulsions, nanoemulsions, and microemulsions; therefore, nanoemulsions are a class of emulsions. The small and fine size of the droplet in nanoemulsions (i.e. droplet diameter <100nm) make them applicable in some fields, due to their enhanced bioavailability, solubility, better stability against gravitational separation, appropriateness for delivery of lipophilic active agent's components, high surface area per unit volume and antimicrobial property. Also, they need less surfactant in comparison with other constructions. There are many kinds of preparation methods that can be classified into low-intensity and high-intensity approaches. The basis of the high-intensity procedure is mechanical energy that comes from flows like cavitation, but the low-intensity procedure is based on physicochemical processes. The most notable ways in high-energy emulsification are high-pressure valve homogenization, microfluidization, ultrasonication, rotor-stator emulsification, and membrane emulsification. Low-energy emulsification is divided into thermal and isothermal methods for nanoemulsions fabrication. Thermal methods consist of phase inversion temperature (PIT) and isothermal methods consist of spontaneous emulsification (SE) and emulsion phase inversion (EPI). Also, today, there is a lot of evidence to compare the low-intensity approach with high-intensity one and some of them express that in the low-energy method, equipment is not expensive and special and this is a very important advantage in saving energy. Also, some researchers express that in the high-energy method, we need much less concentration of surfactant for the formation of small size droplet.

1. Introduction

The science and technology of emulsions are important in many industries, in the particular food industry. Many of the natural or processed foods contain emulsions in the whole material matrix or a part of it as emulsions or have an emulsion phase during the fabrication process. Emulsions are being increasingly used as a receptive system for lipophilic compartments and ingredients like functional foods, colors, flavors, preservatives, vitamins, and medicine. The emulsion-based receptive systems are designed for encapsulating, preserving and releasing these functional segments to increase their management, stability, and effect. Therefore, food products based on emulsion and receptive systems project a wide range of physical, chemical, sensory and biological properties. An emulsion is composed of two insoluble liquids commonly water or oil– where one liquid is dispersed in the other as small spherical droplets. Emulsions can be easily classified based on the water and oil phases' distribution. When oil droplets are dispersed in the water phase, the system is called oil-in-water (O/W) emulsion, like milk, cream, and dressings. The other system entails water droplets dispersed in the oil phase (1) which is called water-in-oil (W/O) emulsion, for example, margarine and butter. Moreover, in addition to

---

*Corresponding author: Department of Food Science and Technology, Science and Research Branch, Islamic Azad University, Tehran, Iran.
E-mail address: dr.h.ahari@gmail.com (Hamed Ahari)

the two mentioned systems, another kind of basic structure made of emulsions includes different kinds of multiple emulsions like oil in water in oil (O/W/O) or water in oil in water (W/O/W). As an instance, water in oil in water emulsion is made of water droplets dispersed in big oil droplets which in turn are dispersed in a continuous water phase. Emulsions are classified based on their droplet's diameter and their thermodynamic stability into conventional emulsions, Nanoemulsions, and micro-emulsions (2). The conventional emulsions which are known as macroemulsions have droplets with a diameter between 100 nm to 100 μm. This kind of emulsions tends to be optically turbid or opaque as the size of their droplets is similar to the visible light wavelength (d= λ) and they strongly scatter light (3). Both macroemulsions and nanoemulsions are thermodynamically unstable, i.e. the droplets in nanoemulsions are smaller than the previous conventional emulsions, although there are some discussions about the other particles in emulsions and nanoemulsions. nanoemulsions are a class of emulsions with very small droplet diameters and therefore, the theory seems clear or semi-clear and are very stable (4). Hence, nanoemulsions can be defined as emulsions with an average diameter of 20-200 nm and this system includes water phase, an oil phase and surfactants that are thermodynamically unstable. This instability is the result of the undesirable molecular interaction in the interfacial area between water and oil due to hydrophobic effect and with time, in order to lessen the surface tension of the phases, they become unstable spontaneously. Consequently, nanoemulsions are always destabilized or broken down through different mechanisms such as Oswald ripening, droplets flocculation, coalescence, and gravitational separation (5, 6). However, it should be noted that, in general, nanoemulsions are more stable against gravitational separation than conventional emulsions since the very small size of particles makes the Brownian force completely overcome the gravitational force (7, 8). Nanoemulsions are also one of the systems which can increase functionality and bioavailability of active agents and enhance their stability. They also have some physicochemical and physiological features that make them suitable for some applications such as encapsulating capability, receiving lipophilic parts like nutraceuticals, flavor, medicine, antioxidants and antimicrobial factors, the release of active agents, which are all bound to their small particle size and larger surface (9, 10). Microemulsions are stable thermodynamic systems i.e. they are spontaneously formed given sufficient time that have particles with a diameter less than 100nm or more precisely between 5 to 50nm (11, 12). Microemulsions are thermodynamically stable systems that contain droplets with the diameter under 100 nm or exactly between 5-50 nm. Microemulsions have particle sizes like nanoemulsions which consequently gives them good stability against gravitational separation which leads to the formation of systems which are optically clear or very little turbid which is due to the weak reflection of light and this is an advantage for they used in some of foods and beverages (13). Additionally, there is a fundamental difference between microemulsions and nanoemulsions: Microemulsions are equilibrium systems –i.e. they are thermodynamically stable– while nanoemulsions are instable systems which tend to spontaneously separate from the forming phase (14). Although nanoemulsions constitute a subcategory of emulsions, they have features that differentiate them from emulsions, for example, nanoemulsions might be optically clear due to the weaker reflection of smaller droplets; nanoemulsions might be highly stable in terms of phase separation with gravity which is because of their weak gravitational forces and Brownian motion force; nanoemulsions can have a higher bioavailability than emulsions (6, 13, 15). New definitions of nanotechnology is the realization and control of materials in 1 to 100nm size, the unique phenomena of which have made a novel and fascinating applications possible (16).

2. Nanoemulsions fabrication methods

Although nanoemulsions are thermodynamically unstable systems, they can be considered as synthetic stability solutions due to their small droplets sizes and their long-lasting stability. This is to means that, the preparation of nanoemulsions requires an amount of free energy. This free energy can be supplied by both mechanical devices and chemical potential systems. Nanoemulsions can be supplied using some of the methods which are commonly classified into low-energy and high-energy methods. In high-energy methods, the energy required for breaking and mixing the oil and water phases comes from the mechanical forces employed in the system (such as tension, turbulence, and cavitation) and the most important mechanical devices used in the fabrication of nanoemulsions are high-pressure valve homogenization, microfluidization, ultrasonication, rotor-stator emulsification, and membrane emulsification. On the other hand, in low-energy methods, most of the free energy of emulsions formation comes from the physicochemical processes (14, 17). Some scholars have reviewed that the low-energy methods can be divided into thermal and non-thermal approaches; where non-thermal methods are related to changes in the composition and include spontaneous emulsification (SE) and emulsion phase inversion (EPI), while thermal methods are based on temperature changes in producing small particles which include phase inversion temperature (PIT) (10).

2.1. High-energy methods

Among the advantages of high-energy methods which sometimes gives them superiority over the low-energy ones, it can be referred to the less usage of surfactant to oil (18), using natural emulsifiers, usage in industrial and large scales, the vastly available equipment and apparatuses (1), as well as the production of highly condensed and stable systems (19), the viscosity of used materials and the low or high level of them, can be decisive for the method or the device being employed, and here we have a brief look at the important processes:

2.1.1. Rotor-Stator Emulsification

The rotor-stator mixer head is made of a rotor mounted on a shaft and a stator are outside it. Rotor functions as a propeller in a centrifugal pump. Fluid enters the rotor axis along with the rotor shaft. Rotor first accelerates the liquid tangentially and then its fluid guidance blade accelerates the fluid through the slot in the stator screen which in turn decreases the size of the droplets (20).

2.1.2. *High-pressure valve homogenization*

A pump is installed in this device which transforms the pre-emulsion to nanoemulsions using a tiny drop distribution with very high pressure of 50-200MP. This means that the mixture is affected by the high pressure and by passing through the small valve it is pumped. This very high sheer tension results in the formation of very small particles (21, 22).

2.1.3. *Microfluidization*

The intended materials enter the system through the inlet reservoir and get injected into the reaction chamber with a high inlet pressure of 100-300MPa, producing very small particles. High-speed flows are applied for the production of ultra-small particles that cavitation is one of such techniques.

2.1.4. *Ultrasonication*

Another method in the production of nanoemulsions is ultrasonication. Nano-emulsions are usually made through ultrasonication using an apparatus that is composed of a probe, a metal horn and a generator (the standard frequency of 20-24 kHz) and a piezoelectric transducer. A piezoelectric transducer is a device that converts the electrical oscillations to mechanical oscillations with a similar frequency. The mechanical vibrations produced by the piezoelectric transducer are amplified and guided using a metal horn and then transformed into acoustic waves at its tip. The ultrasound waves are transmitted to the fluid where the oscillatory acoustic pressure is induced (23). The high-pressure waves produced by ultrasonic transducer create small bubbles near the probe tip which are in great oscillations and then they destabilize and are blown from inside. As a result of this blast, intense shear forces and chaos are created. This form of acoustic cavitation is one of the most important factors that lead to the formation of small droplets in nanoscale during homogenization (24).

2.1.5. *Membrane emulsification*

The fabrication of emulsion directly from two separate liquids by passing a liquid (disperse or internal phase) through the membrane from another immiscible liquid (continuous or external phase) is called direct membrane emulsification (25).

2.2. *Low-energy methods*

Low-energy methods are mainly either based on the release of chemical materials from the formulation components and compositions (26) or due to the spontaneous formation of droplets in the border between water and oil phase which is highly dependent on the nature of the surface-active molecules and their molecular stability and geometry. In the recent years, emulsification methods with low energy have attracted a lot of attention as they can fabricate extremely small emulsions with low operational costs and less capital for equipment than high-energy methods (27), which include the following:

2.2.1. *Spontaneous emulsification*

This is one of the low-energy methods that happen when two miscible liquids with different levels of free energy are in touch. That is to mean that there is an organic phase which has been poured into the water phase and been mixed with it, a homogenized oil solution together with the organic phase, a lipophilic surfactant and a solvent which is miscible with water and a water phase containing water and hydrophilic surfactant (28).

2.2.2. *Emulsion phase inversion (EPI)*

This is a low-energy method which includes the addition of water phase to oil phase while stirring. This usually contains oil and surfactant. This seems that based on the conducted researches, the basis of EPI is the catastrophic change or inversion of phase (29). When first the water phase is titrated into the organic phase, water in oil emulsion is formed and when more water is added, a liquid crystal phase might be formed which can be very viscous and stop the constant stirring. This seems that the formation of crystal phase is the most important intermediate step in nanoemulsions fabrication which results in the production of a constant two-layer Microemulsions which ultimately breaks and then, very smaller droplets are formed (30). When more water is added, multiple emulsions (O/W/O) are formed and the system viscosity decreases. The fabrication of these multiple emulsions is another important intermediate stage in the preparation of oil in water emulsion or nanoemulsion (31).

2.2.3. *Phase inversion temperature (PIT)*

This method, like the other low-energy methods, does not require specialized apparatuses and for the formation of nanoemulsions, a hydrophilic nonionic surfactant, oil, and water are mixed in main stages. This procedure leads to the distribution of bicontinuous microemulsions which leads to the production of small oil droplets (32) and oil in water nanoemulsions are fabricated (26).

3. Nanoemulsions applications in the food industries

In the past decades, there was a vast interest in using nanoparticles and nanoemulsions distribution for a variety of medical and industrial applications like pharmaceuticals, food, agriculture chemistry, cosmetics, and self-care industries. Some of the important applications of nanoemulsions are as follows:

i. Antimicrobial properties of nanoemulsions: Many of the present chemicals approved as antimicrobials used in foods are water-soluble, therefore, they are not suitable for connecting to oil droplets in nanoemulsions. In such cases, encapsulating antimicrobial materials in nano-emulsions might enhance their practicality and effectiveness. The antimicrobial factor can be encapsulated with internal hydrophobic oil droplets or external amphiphilic ones or both (33).

ii. Bioactive nanoemulsions: due to the capability of nanoemulsions for improving the solubility of biological compositions and also the capability of being absorbed in the gut which is penetrable by surfactants, they are suitable options for delivering water-insoluble food additives and lipophilic compositions. Many bioactive materials such as many vitamins and nutraceuticals which are considered food complements are lipophilic; hence, they are usually emulsified before being incorporated in food structure (34).

iii. Nanoemulsions as receptive and transmitting systems: During the past years, the interest in using nanoemulsions as receptive systems of lipophilic factors in foods and beverages as increased which is attributed to their high physical stability, high bioavailability and their transparency (35).

iv. Nanoemulsions used in edible packaging: For many years, edible packing has been used as a physical barrier between the environment and foodstuff for controlling the mass transfer and extending the shelf life. Nevertheless, today, using nanoemulsions, edible packaging which contains active food components in their formula can strengthen their practical function in addition to the inhibitory factor (36).

Kentish et al. (37) utilized the ultrasonic method for preparing nanoemulsions. This goes without saying that oil-water emulsions are important carriers for receiving hydrophobic bioactive materials in a range of food ingredients. Additionally, nowadays there is a vast interest in the production of very small emulsions in the beverage industry so that these new elements can be added with a slight effect on the transparency and clarity of the solution. In the present research, both the batch method and the focused flow-through ultrasonic of particles were used in emulsification with 20-24 KHz power. Emulsions with the least particle sizes of 135 ± 5nm were obtained using cotton oil and water in the presence of Tween 40 surfactant. The obtained results were compared with the emulsions produced using the microfluidizer method is 100MPa. The fundamental point for making ultrasonic emulsification efficient in determining the optimum inlet ultrasonic energy intensity of these systems, because if the inlet power is excessive, it can cause increase in the size of the droplets. Leong et al. (24) worked on the decrease of oil droplets size using ultrasonic emulsification. These scholars expressed that the efficient production of nanoemulsions with droplets sizes of less than 100nm facilitates the addition of bioactive agents to water-based foods. The small size of droplets causes the production of transparent emulsions, while the appearance of the product does not change by adding an oil phase. This study demonstrated that significant small and lucid O/W nanoemulsions with a diameter of less than 40nm can be created with sun water oil. This is possible using ultrasound or high shear homogenization, surfactant/cosurfactant/oil system which is well optimized. This less than 40nm diameter of droplets is obtained when both droplets deformability (surfactant design) and the shear employed (equipment geometry) are optimized. Also, the time needed for reaching this minimum droplet size was affected by equipment configuration. The results in atmosphere pressure show a meaningful relationship with the total energy density. They also concluded that this relationship changes when pressure higher than 400kPa is exerted on the sonication reservoir and leads to the fabrication of efficient emulsion. Besides, oil stability is not affected by the ultrasound process (24). Ostertag et al. (38) stated that nanoemulsions can be used for encapsulation and being the oral delivery reception of bioactive lipophilic compositions like medicines and nutraceuticals. Today, an increasing interest exists in using low-energy methods in producing edible nanoemulsions. This research examined the effect of mixing and the reaction conditions in the formation of edible nanoemulsions using the Emulsion Phase Inversion (EPI) method. EPI method includes aqueous phase (water) to organic phase (oil + hydrophilic surfactant) titration. The effect of oil and surfactant types, the surfactant to oil ratio (SOR) and the initial position of surfactant on the distribution of emulsion particle size were studied. The size of the droplets produced through this method depends on; (a) oil type: medium-chain triglycerides < flavor oils (orange and limonene) < long-chain triglycerides (olive, grape, sesame, peanut, canola oils), (b) surfactant type: Tween 80 <Tween 20 < Tween 85, (c) surfactant concentration: smaller droplets were prepared in higher SOR, (d) surfactant position: surfactant initially in oil < surfactant initially in water. Moreover, low-energy-method (EPI) was compared with the high-energy method (microfluidization); accordingly, the small droplets (d<160nm) could be produced with both methods, but a very low amount of surfactant was needed for the high-energy method (0.1≤ SOR)as compared with the low-energy method (0.7≤ SOR).

Li et al. (39) conducted research aimed to optimize the process and stability of D-limonene nanoemulsions. These nanoemulsions were prepared using a catastrophic phase inversion method which is one of the low-energy methods, with Tween 80 as a surfactant. According to the results, the SOR index (surfactant to oil ratio) can significantly affect the opacity and mean diameter of emulsion particles. In the highest concentration of surfactant (1, 5), D-Limonene nanoemulsions can be obtained. Additionally, the formation of nanoemulsions may be firstly related to the oil phase viscosity. When the oil phase contains less than 15 % (W/W) of olive oil, the nanoemulsions can be fabricated. the opacity and mean diameter of nanoemulsions particles were similar to the equal concentration of herbal oils. Besides it can be said that the addition of olive oil can enhance the stability of the D-Limonene nanoemulsions system and lower the Ostwald ripening level.

4. Conclusion

Nowadays, due to their small-sized droplets, nanoemulsions have unique features like clarity and carrier systems for bioactive composition which makes them suitable for usage in many foods, particularly for functional foods and nutraceuticals. Nanoemulsions are thermodynamically unstable which is related to the interactional molecular effect on the interfacial area of water and oil due to the hydrophobic effect. Over time, they have the tendency to become stable through some mechanisms which by decreasing the size of droplets prohibits the break of molecules and stabilizes them. On the other hand, this size of droplets gives them antimicrobial property against a vast range of bacteria and yeasts which is of importance for enhancing the shelf life and safety of food products. During the recent years, the methods for fabricating nanoemulsions using high-energy and low-energy techniques and particularly the isothermal approach has captured special attention, but as there is lack of sufficient information about some of the significant and influential factors acting on their formation and stability, or scholars have not yet reached a consensus about the order and amount of adding materials such as organic and water phases or surfactant and cosurfactant which are different regarding each method, there exists considerable interest in researching these parameters. The important variables about the size of the droplets produced through low-energy methods include a surfactant to oil ratio, surfactant type, surfactant position, and the oil type. This also has to be noted that all low-energy methods can have one similar mechanism in common which entails the movement of surfactant from oil phase to aqueous phase to form tiny emulsion droplets in the water and oil interface. The biggest drawback of low-energy methods in producing nanoemulsions is using a large amount of surfactant which is nevertheless, still cost-effective as compared with the expensive methods and specialized apparatuses in high-energy methods. Besides, different high-energy methods are fundamentally various in terms of how they control high viscosity dispersions. For instance, high-pressure valve homogenizer and microfluidizer are suitable for products with low viscosity and membrane emulsification for medium density materials, this is while high viscosity materials are the most suitable for rotor-stator apparatus. Moreover, the results of researches indicate that cavitation is one of the most important and common mechanisms in high-energy methods applied on dispersion systems which include two phases dispersed in each other and air bubbles. The drop in static pressure causes expansion in the bubbles and if this frequency, periodicity, and range of these oscillations are large enough, the contraction stages gradually lead to a sudden collapse which blows the bubbles from inside.

Acknowledgments

This work was supported by the Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran.

References

1. McClements DJ. Food emulsions: principles, practices, and techniques: CRC press; 2015.
2. McClements DJ. Emulsion design to improve the delivery of functional lipophilic components. *Annual Review of Food Science and Technology*. 2010;1:241-69.
3. Tadros TF, Vandamme A, Levecke B, Booten K, Stevens C. Stabilization of emulsions using polymeric surfactants based on inulin. *Advances in Colloid and Interface Science*. 2004;108:207-26.
4. Pey C, Maestro A, Solé I, González C, Solans C, Gutiérrez JM. Optimization of nano-emulsions prepared by low-energy emulsification methods at constant temperature using a factorial design study. *Colloids and Surfaces A: Physicochemical and Engineering Aspects*. 2006;288(1-3):144-50.
5. McClements DJ, Xiao H. Potential biological fate of ingested nanoemulsions: influence of particle characteristics. *Food & Function*. 2012;3(3):202-20.
6. Jafari SM, McClements DJ. Nanoemulsions: Formulation, applications, and characterization: Academic Press; 2018.
7. McClements DJ. Biopolymers in food emulsions. Modern Biopolymer Science: Elsevier; 2009. p. 129-66.
8. Wooster TJ, Golding M, Sanguansri P. Impact of oil type on nanoemulsion formation and Ostwald ripening stability. *Langmuir*. 2008;24(22):12758-65.
9. Kesisoglou F, Panmai S, Wu Y. Application of nanoparticles in oral delivery of immediate release formulations. *Current Nanoscience*. 2007;3(2):183-90.
10. Komaiko JS, McClements DJ. Formation of food-grade nanoemulsions using low-energy preparation methods: A review of available methods. *Comprehensive Reviews in Food Science and Food Safety*. 2016;15(2):331-52.
11. Garti N, Benichou A. Recent developments in double emulsions for food applications. *Food Emulsions*. 2004;35.
12. Van der Sman R, Van der Graaf S. Diffuse interface model of surfactant adsorption onto flat and droplet interfaces. *Rheologica Acta*. 2006;46(1):3-11.
13. McClements DJ. Fabrication, characterization and properties of food nanoemulsions. Nanotechnology in the Food, Beverage and Nutraceutical Industries: Elsevier; 2012. p. 293-316.
14. Solans C, Esquena J, Forgiarini AM, Uson N, Morales D, Izquierdo P, et al. Nano-emulsions: formation, properties, and applications. *Surfactant Science Series*. 2003;109:525-54.
15. Lu WC, Huang DW, Wang CC, Yeh CH, Tsai JC, Huang YT, et al. Preparation, characterization, and antimicrobial activity of nanoemulsions incorporating citral essential oil. *Journal of Food and Drug Analysis*. 2018;26(1):82-9.
16. Wang G. Nanotechnology: The new features. arXiv preprint arXiv:181204939. 2018.
17. Tadros T, Izquierdo P, Esquena J, Solans C. Formation and stability of nano-emulsions. *Advances in Colloid and Interface Science*. 2004;108:303-18.
18. Ozturk B, Argin S, Ozilgen M, McClements DJ. Formation and stabilization of nanoemulsion-based vitamin E delivery systems using natural surfactants: Quillaja saponin and lecithin. *Journal of Food Engineering*. 2014;142:57-63.
19. Jafari SM, He Y, Bhandari B. Optimization of nano-emulsions production by microfluidization. *European Food Research and Technology*. 2007;225(5-6):733-41.
20. Mortensen HH, Calabrese RV, Innings F, Rosendahl L. Characteristics of batch rotor–stator mixer performance elucidated by shaft torque and angle resolved PIV measurements. *The Canadian Journal of Chemical Engineering*. 2011;89(5):1076-95.
21. Quintanilla-Carvajal MX, Camacho-Díaz BH, Meraz-Torres LS, Chanona-Pérez JJ, Alamilla-Beltrán L, Jimenéz-Aparicio A, et al. Nanoencapsulation: a new trend in food engineering processing. *Food Engineering Reviews*. 2010;2(1):39-50.
22. Sanguansri P, Augustin MA. Nanoscale materials development–a food industry perspective. *Trends in Food Science and Technology*. 2006;17(10):547-56.3.

23. Feng H, Yang W. Ultrasonic processing. Nonthermal processing technologies for food: Wiley-Blackwell and IFT Press, UK; 2011. p. 135-54.
24. Leong T, Juliano P, Knoerzer K. Advances in ultrasonic and megasonic processing of foods. *Food Engineering Reviews*. 2017;9(3):237-56.
25. Piacentini E, Drioli E, Giorno L. Membrane emulsification technology: Twenty-five years of inventions and research through patent survey. *Journal of Membrane Science*. 2014;468:410-22.
26. Anton N, Vandamme TF. The universality of low-energy nano-emulsification. *International Journal of Pharmaceutics*. 2009;377(1-2):142-7.
27. Date AA, Desai N, Dixit R, Nagarsenker M. Self-nanoemulsifying drug delivery systems: formulation insights, applications and advances. *Nanomedicine*. 2010;5(10):1595-616.
28. Bouchemal K, Briançon S, Perrier E, Fessi H. Nano-emulsion formulation using spontaneous emulsification: solvent, oil and surfactant optimization. *International Journal of Pharmaceutics*. 2004;280(1-2):241-51.
29. Zhang T, Xu Z, Cai Z, Guo Q. Phase inversion of ionomer-stabilized emulsions to form high internal phase emulsions (HIPEs). *Physical Chemistry Chemical Physics*. 2015;17(24):16033-9.
30. Hategekimana J, Zhong F. Degradation of vitamin E in nanoemulsions during storage as affected by temperature, light and darkness. *International Journal of Food Engineering*. 2015;11(2):199-206.
31. Jahanzad F, Crombie G, Innes R, Sajjadi S. Catastrophic phase inversion via formation of multiple emulsions: a prerequisite for formation of fine emulsions. *Chemical Engineering Research and Design*. 2009;87(4):492-8.
32. Saberi AH, McClements DJ. Fabrication of protein nanoparticles and microparticles within water domains formed in surfactant–oil–water mixtures: Phase inversion temperature method. *Food Hydrocolloids*. 2015;51:441-8.
33. Weiss J, Gaysinsky S, Davidson M, McClements J. Nanostructured encapsulation systems: food antimicrobials. Global Issues in Food Science and Technology: Elsevier; 2009. p. 425-79.
34. Salvia-Trujillo L, Soliva-Fortuny R, Rojas-Graü MA, McClements DJ, Martin-Belloso O. Edible nanoemulsions as carriers of active ingredients: A review. *Annual Review of Food Science and Technology*. 2017;8:439-66.
35. McClements DJ, Rao J. Food-grade nanoemulsions: formulation, fabrication, properties, performance, biological fate, and potential toxicity. *Critical Reviews in Food Science and Nutrition*. 2011;51(4):285-330.
36. Acevedo-Fani A, Soliva-Fortuny R, Martín-Belloso O. Nanoemulsions as edible coatings. *Current Opinion in Food Science*. 2017;15:43-9.
37. Kentish S, Wooster T, Ashokkumar M, Balachandran S, Mawson R, Simons L. The use of ultrasonics for nanoemulsion preparation. *Innovative Food Science & Emerging Technologies*. 2008;9(2):170-5.
38. Ostertag F, Weiss J, McClements DJ. Low-energy formation of edible nanoemulsions: factors influencing droplet size produced by emulsion phase inversion. *Journal of Colloid and Interface Science*. 2012;388(1):95-102.
39. Li Y, Zhang Z, Yuan Q, Liang H, Vriesekoop F. Process optimization and stability of d-limonene nanoemulsions prepared by catastrophic phase inversion method. *Journal of Food Engineering*. 2013;119(3):419-24.