REVIEW ARTICLE

A Critical Review on Nanoemulsion: Advantages, Techniques and Characterization

Gunjan P. Malode*, Sarin A. Chavhan, Shivam A. Bartare, Lochana L. Malode, Jagdish V. Manwar, Ravindra L. Bakal

Abstract

Nanoemulsions have small droplet size and are kinetically stable colloidal systems. These are the thermodynamically stable isotropic system in which two immiscible liquids are mixed to form a single phase by means of appropriate surfactant and cosurfactant. Nanoemulsion droplet sizes fall typically in the range of 20–200 nm and shows narrow size distribution. They have enhanced functional properties in comparison to conventional emulsions. The composition and structure of the nanoemulsions can be controlled for the encapsulation and effective delivery of bioactive lipophilic compounds. Nanoemulsions have potential application in the food industry for the delivery of nutraceuticals, coloring and flavoring agents, and antimicrobials. This review aims to provide consolidated information regarding various formulation and characterization techniques developed for nanoemulsions. Various characterization techniques for nanoemulsions include determination of entrapment efficiency, particle size, polydispersity index, zeta potential as well as characterization through differential scanning calorimetry, Fourier-transform infrared spectroscopy and transmission electron microscopy.

Keywords: *Bioavailability, Characterization techniques, Nanoemulsions, Self-emulsifying formulation, Self-nanoemulsifying drug delivery systems.*

Journal of Applied Pharmaceutical Sciences and Research, (2022); DOI: 10.31069/japsr.v4i3.2

Introduction

Emulsions are defined as the dispersion of two immiscible liquids, with the spherical droplets forming the dispersed phase, whereas the liquid surrounding it forms the continuous phase.[1,2] The oil droplets dispersed in an aqueous phase are known as oil-in-water (o/w) emulsions and it can be used for the delivery of hydrophobic active substances. The water droplets dispersed in oil are called the water-in-oil (w/o) emulsions and it is used for the delivery of hydrophilic compounds. Multiple emulsion systems can also be developed in water-in-oil-in-water (w/o/w) and oil-in-water-in-oil (o/w/o) emulsions. The w/o/w emulsions are made of large oil droplets, containing water droplets dispersed in an aqueous phase. Whereas, in o/w/o emulsion system, water droplets containing oil droplets are dispersed in an oil phase. Bicontinuous nanoemulsion contains microdomains of oil and water—inter-dispersed within the system.[3,4] In Table 1, a variety of types of emulsion systems have been mentioned. However, there is some ambiguity regarding their description based on size[5]. Nanoemulsion drug delivery systems are a shows potential tool for delivering and improving the bioavailability of hydrophobic drugs and bioactive food components present in the blood fluid. The majority of drugs are hydrophobic (lipophilic) in nature, thus leads to low solubility and bioavailability problems.[6,7]

An emulsion is a biphasic system in which one phase is intimately dispersed in the other phase in the form of minute droplets ranging in diameter from 0.1 to 100 lm. It is a thermodynamically unstable system, which can be stabilized by the presence of an emulsifying agent (emulgent or emulsifier). Two types of phases in in emulsion i.e., dispersed phase and dispersion medium. The dispersed phase is also called as internal phase or the discontinuous phase while the outer phase is known dispersion medium, external phase or continuous phase. The emulsifying agent used in it also known as intermediate phase or inter phase.[8]

IBSS's Dr. Rajendra Gode Institute of Pharmacy, Amravati-444 602, Maharashtra, India

Corresponding Author: Gunjan P. Malode, IBSS's Dr. Rajendra Gode Institute of Pharmacy, Amravati-444 602, MS, India, Email: gadgegunjan96@gmail.com

How to cite this article: Malode GP, Chavhan, SA, Bartare SA, Malode LL, Manwar JV, Bakal RL. A Critical Review on Nanoemulsion: Advantages, Techniques and Characterization. Journal of Applied Pharmaceutical Sciences and Research. 2021; 4(3):6-12.

Source of support: Nil

Conflict of interest: None

Nanoemulsion

Nanoemulsion may be defined as a colloidal dispersion of two immiscible liquids that is thermodynamically unstable with each other. In nanoemulsion, one of the liquids forms the dispersed phase and other liquid forms the dispersing medium[9]. Nanoemulsion comprise droplets with diameters ranging from 10~200 nm and each droplet has a protective coating of emulsifier molecules.[10-13] The nanoemulsions have droplet dimensions like the microemulsions ranging from <200 and in some cases <100nm.[14] Like conventional emulsions, nanoemulsions are thermodynamically metastable as phase separation occurs over time. However, nanoemulsions are conferred with kinetic stability as there

Table 1: Types of Emulsion with respect to parameters

Parameters	*Emulsion/ Coarse emulsion/ Macroemulsion*	*Microemulsion*	*Nanoemulsion*
Size	1–10 μM	10–100 nm	<200 nm
Thermodynamic Stability	Metastable	Stable	Metastable
Kinetic Stability	Stable	Unstable	Stable
Optical property	Turbid	Transparent	Transparent
Polydispersity	High	Low	Low
Preparation Method	High and low energy methods	Low energy Methods	High and low energy methods
Effect of temperature and PH	Stable to temperature and pH changes	Effect by changes in temperature and pH	Stable to temperature and pH changes

is no gravitational separation and droplet aggregation due to the reduced attractive force between the small sized droplets.[15]

The present review focuses on the increased application of nanoemulsions in the food industries for sustainable food processing and packaging. The nanoemulsions can encapsulate functional compounds and active ingredients including antioxidants and nutraceuticals. They are also useful in the controlled release of flavor compounds in foods.[15,16] Nanoemulsion encapsulation of bioactive compounds increase its solubility, controlled release and absorption in the gastrointestinal tract, and absorption through cells.[15,17] Nanoemulsion based edible nanocoatings containing flavor and coloring ingredients, antioxidants, enzymes, antimicrobials, and antibrowning agents can be used to coat foods such as meats, dairy products such as cheese, fresh produce, and fresh cuts including fruit and vegetables and confectionaries to improve their shelf life. The nanoemulsion coatings can also prevent moisture and gas exchange, minimize moisture loss and oxidation of foods.[18-21]

The term 'nanoemulsion' also refers to a miniemulsion which is fine oil/water or water/oil dispersion stabilized by an interfacial film of surfactant molecule having droplet size range 20–600 nm. Because of small size, nanoemulsions are transparent. There are three types of nanoemulsion which can be formed:

- Oil in water nanoemulsion in which oil is dispersed in the continuous aqueous phase,
- Water in oil nanoemulsion in which water droplets are dispersed in continuous oil phase, and
- Bi- continuous nanoemulsions.[19,21]

Advantages of Nanoemulsion[20-22]

- Nanoemulsions have higher surface area and free energy that make them an effective transport system.
- They do not show the problems of inherent creaming, flocculation, coalescence, and sedimentation.
- It can be formulated in variety of formulations such as foams, creams, liquids, and sprays.
- They are non-toxic, non-irritant hence can be easily applied to skin and mucous membranes.
- It can be administered orally if the formulation contains surfactants which are biocompatible.
- It do not damage healthy human and animal cells hence are suitable for human and veterinary therapeutic purposes.
- It provides better uptake of oil-soluble supplements in cell cultures technology to improve growth of cultured cells and allows toxicity studies of oil-soluble drugs.
- It may be applied as a substitute for liposomes and vesicles, and it is possible to build lamellar liquid crystalline phases around the nanoemulsion droplets.[1]
- Due to their small size, nanoemulsions can penetrate through the "rough" skin surface and this enhances penetration of actives.
- It constitutes the primary step in nanocapsules and nanospheres synthesis using nano precipitation and the interfacial polycondensation.

Self-emulsifying Formulation

Self-emulsifying formulations comprise of self-emulsifying drug delivery systems (SEDDS) and self-nanoemulsifying drug delivery systems (SNEDDS). SEDDS give coarse emulsion whereas SNEDDS provide nano-size emulsion. These systems are isotropic mixtures of an oil, surfactant, and co-surfactant. Upon *in vivo* dilution by the aqueous phase, these systems form emulsions (in case of SEDDS) or fine and optical clear nanoemulsions (in case of SNEDDS) under gentle agitation, experienced due to gastrointestinal tract (GIT) motility. SEDDS and SNEDDS are generally described as emulsion or nanoemulsion pre-concentrates because the emulsion or nanoemulsion is formed from dilution in aqueous media *in vivo*.[23,24]

Techniques of Preparation of Nanoemulsions

The most used methods for producing nanoemulsions are as follows:

- High-Pressure Homogenization
- Microfluidization
- Ultrasonication
- Phase inversion method
- Spontaneous Emulsification
- Solvent Evaporation Technique
- Hydrogel Method

High Pressure Homogenization[25,26]

The preparation of nanoemulsions requires high-pressure homogenization. This technique makes use of high-pressure homogenizer/ piston homogenizer to produce nanoemulsions of extremely low particle size (up to 1-nm) (Figures 1 and 2). The dispersion of two liquids (oily phase and aqueous phase) is achieved by forcing their mixture through a small inlet orifice at very high pressure (500 to 5000 psi), which subjects the product to intense turbulence and hydraulic shear resulting in extremely fine particles of emulsion .The particles which are created exhibit a liquid, lipophilic core separated from the surrounding aqueous phase by a monomolecular layer of phospholipids.

Advantages

- Ease of scale-up and little batch-to-batch variation.
- Narrow size distribution of the nanoparticulate drug.
- Flexibility in handling the drug quality.
- Effectively used for thermolabile substances.

Disadvantage

High energy consumption and increase in temperature of emulsion during processing.

Microfluidization[27]

Micro-fluidization is a mixing technique, which makes use of a device called micro-fluidizer (Figure 3). This device uses a highpressure positive displacement pump (500 to 20000 psi), which forces the product through the interaction chamber, which consists of small channels called micro-channel. The product flows through the micro channels on to an impingement area which results in very fine particles of sub- micron range. The two solutions i.e., aqueous phase and oily phase are combined and processed in an in turn to homogenizer to yield a coarse emulsion formed. The coarse emulsion is into a micro-fluidizer where it is further processed to obtain a stable nanoemulsion. The coarse emulsion is passed through the interaction chamber micro-fluidizer repeatedly until desired particle size is obtained through it. The bulk emulsion is then get filtered through a filter under nitrogen to remove large droplets present in it and this results in a uniform nanoemulsion.

Ultrasonication[28,29,30]

The preparation of nanoemulsion is reported in various research papers which aim to use the ultrasonic sound frequency for the reduction of the droplet size. The best approach is that the use of a constant amplitude sonotrode at system pressures in excess of the ambient value. It is well known that increasing the external pressure increases the cavitations threshold within an ultrasonic field and thus fewer bubbles form. Although, increasing the external pressure also increases the collapse pressure of cavitations bubbles. This means that the collapse of the bubbles when cavitation occurs becomes stronger and more violent than when the pressure is at atmospheric conditions. As cavitation is the most important mechanism of power dissipation in a low frequency ultrasonic system, these changes in navigational intensity can be related directly to changes in the power density. The system also uses a water jacket to control the temperature to optimum level (Figure 4).

Phase Inversion Method[31,32]

In phase inversion method, fine dispersion is obtained by chemical energy resulting of phase transitions produced by emulsification pathway. The phase transition is produced by varying the composition of the emulsion and keeping temperature constant. The phase inversion temperature was first done by, and it was concluded that increase in temperature results in the chemical changes of polyoxyethelene surfactants by degradation of the polymer chain with the temperature. This technique is used for the preparation of o/w nanoemulsion. The main advantage of this system is that it is based on the phase transition that takes place during the emulsification process. In this technique, varying the composition of constituents changes the hydrophilic–lipophilic behavior of emulsifier as shown in Figure 5 and 6.

Spontaneous Emulsification Method

In this technique, spontaneous emulsions are formed on mixing water and oil together with an emulsifier by gentle stirring at a particular temperature (Figure 7). The mixing of phases by gentle magnetic stirring causes the emulsifier to enter the aqueous phase leading to increase of

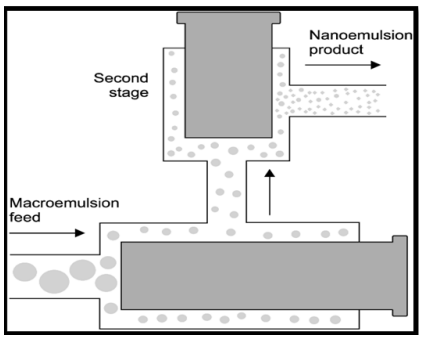

Figure 1: High pressure homogenization showing the formation of nanoemulsion

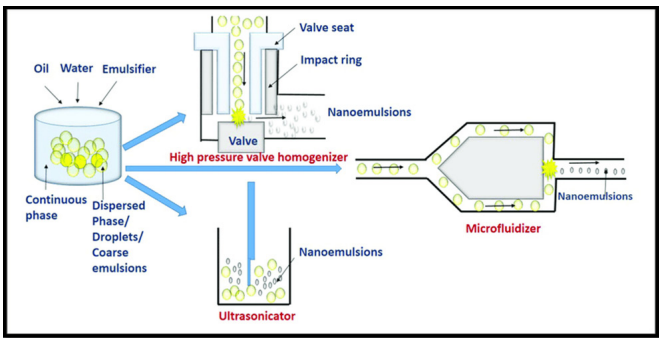

Figure 2: High pressure homogenization (HPH), microfluidizer, and ultrasonication break macroemulsions into smaller droplets

oil-water interfacial area resulting in oil droplet formation.[33] Spontaneous emulsification involves three main steps and they are as follows:

- Preparation of homogeneous organic solution composed of oil and lipophilic surfactant in water miscible solvent and hydrophilic surfactant.
- The organic phase was injected in the aqueous phase under magnetic stirring the o/w emulsion was formed.
- The water-miscible solvent was removed by evaporation under reduced pressure.[34,35]

Solvent Evaporation Technique[36,37]

This technique involves preparing a solution of drug followed by its emulsification in another liquid that is non-solvent for the drug (Figure 8). Evaporation of the solvent leads to precipitation of the drug. Crystal growth and particle aggregation can be controlled by creating high shear forces using a high-speed stirrer.

Hydrogel Method[38,39]

It is similar to the solvent evaporation method. The only difference between the two methods is that the drug solvent is miscible with the drug anti-solvent. Higher shear force prevents crystal growth and Ostwald ripening. Other method used for Nanoemulsion preparation is the phase inversion temperature technique.

Formulation Aspects of Nanoemulsion[40-43]

Formulation of nanoemulsion includes active drug, additives and emulsifier which are as shown in Table 2. The list of most commonly used oils and adsorption enhancers in formulation of nano emulsions is presented in Table 3 and Table 4 respectively.

Factors Affecting the Formulation of Nanoemulsion:[44]

- Appropriate composition is required to avoid Oswald ripening the dispersed phase should be highly insoluble in the dispersed medium.
- The surfactant is an essential part of the Nanoemulsion. They should not form lyotropic liquid crystalline "microemulsion" phases. Systems containing short chain alkanes, alcohols, water, and surfactants form the phases

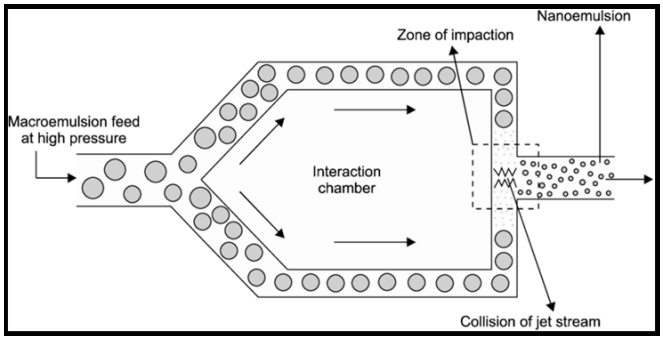

Figure 3: Microfluidization

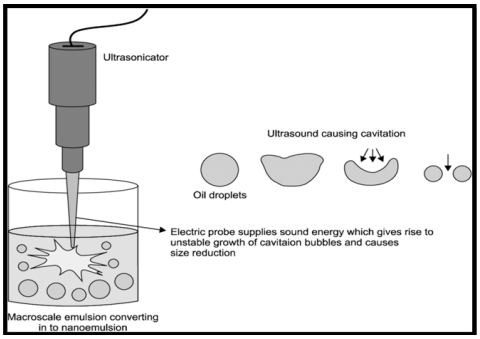

Figure 4: Ultrasonication techniques

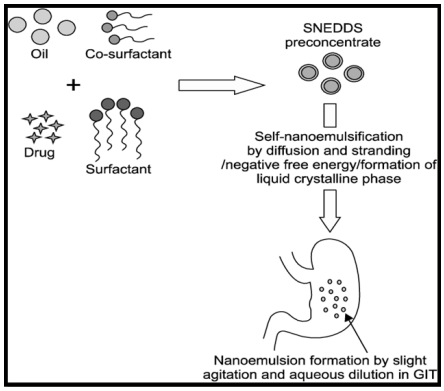

Figure 5: Phase inversion emulsification techniques

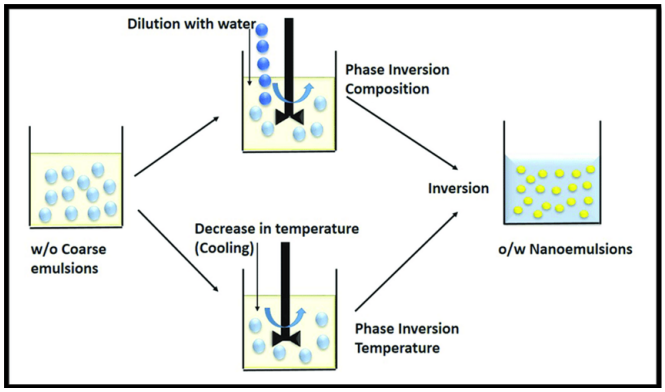

Figure 6: Low energy methods for phase inversion

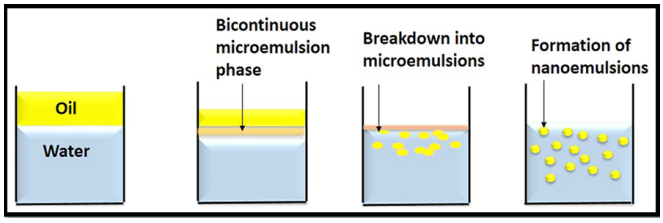

Figure 7: Spontaneous Emulsification Method

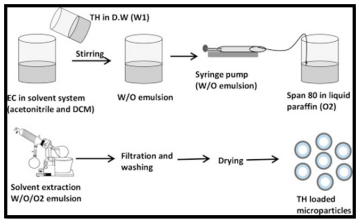

Figure 8: Solvent Evaporation technique

which are used with the co surfactant.

- The presence of excess surfactants enables new surface area of nanoscale to be rapidly coated during emulsification there by inhibiting induced coalescence.
- Extreme share must be applied to rupture microscale droplets to nanoscale by providing the stress level to reach above the Laplace pressure of the droplets with a pressure of 10–100 atm. Out of various methods ultrasonication is widely used in laboratory.

Characterization of Nanoemulsion

The physiochemical properties of nanoemulsions such as physical properties, stabilities, rheological property, and microstructure must be characterized for its application in foods as these properties are known to influence the final texture, taste, flavor, and stability of foods.

The basic physical properties of nanoemulsion are as follows-[45,46].

- Dye Solubilisation
- Dilutability Test
- Conductance Measurement
- Dynamic Light-Scattering measurements
- Polydispersity
- Phase Analysis
- Interfacial Tension
- Viscosity measurement
- pH
- Refractive Index
- Transmission Electron Microscopy
- *In Vitro* Skin Permeation Studies
- Thermodynamic Stability Studies

Current Perspectives and Future Prospects

In the last few years, a number of studies have been conducted to ascertain the advantages of encapsulation of lipophilic and functional compounds in nanoemulsions. Nanoemulsification is known to protect and increase the bioavailability of bioactive compounds as shown by in vitro studies. But there are limited studies which show the actual health benefits of including nanoemulsions in foods, their consumption, labeling, and public perception. Similarly, studies have been conducted to evaluate the use of high or low energy approach to formulate nanoemulsions and the focus is on optimizing processing parameters and ingredients used in nanoemulsion preparation. But there is not much research on reducing the cost of production of nanoemulsions as its preparation and application for fortifying and packaging in foods require higher energy input and equipment investment. Similarly, the risks associated with the use of engineered nanoemulsions in foods is not known.

The potential toxicological effects and biological fate of nanoparticles after digestion has not been elucidated. Nanoemulsions of bioactive compounds and functional food ingredients have an enormous potential for applications in the food industries. The emulsion-based delivery systems and nanoemulsion edible coatings can improve the functionalities of food and enhance their quality and shelf life. Therefore, it is important to optimize the bioactivity of the encapsulated components for scaled up production.

Further studies should focus on the biological events and risks associated with the use of nanoemulsion based delivery systems in food product and packaging application for ensuring safety of the consumers.

Table 2: Formulation table of nanoemulsion

Components	*Examples*
Oils	Castor oil, Corn oil, Coconut oil, Evening primrose oil, linseed oil, Mineral oil, olive oil, peanut oil
Emulsifiers	Natural lecithins from plant or animal source, phospholipids, castor oil Derivatives, polysorbates, sterylamine.
Additives	Lower alcohol (ethanol), propylene glycol, 1, 3-butylenes glycol, sugars such as butylenes glycol, sugars such as glucose, sucrose, fructose, and maltose.
Antioxidants	Ascorbic acid, α-tocopherol.
Surfactant	Polysorbate20, Polysorbate80, Polyoxy 60, castor oil, Sorbitan monooleate, PEG300, Caprylic glyceride
Co-surfactant	Ethanol, glycerine, PEG300, PEG400, Polyene glycol, Poloxamer.
Tonicity modifiers	Glycerol, Sorbitol and xylitol.
pH adjusting agent	Sodium hydroxide or hydrogen chloride.
Preservatives	Methyl Paraben, Propyl Paraben, Benzalkonium Chloride (0.01%w/v)

Table 3: List of oils used in nanoemulsion

Name of Oil	*Manufacturer*	*Chemical Name*
Captex 355	Abitec	Glyceryl Tricaorylate/Caprate
Captex 200	Abitec	Propylene Dicaprylate/Dicaprate Glycol
Captex 8000	Abitec	Glyceryl Tricaprylate (Tricaprylin)
Witpsol	Sasol pharmaceutical excipient	90:10%w/w c12 Glyceridetri:diesters
Myritol 318	Russia	C8/c10 triglycerides
Isopropyl myristate	Fluka	Myristic acid isopropyl ester

Table 4: List of adsorption enhancers

S. No.	*Solubilizing, surfactants, emulsifying agents adsorption enhancers*
1	Capryol 90
2	Gelucire 44/14,50/13
3	Cremophor RH 40
4	Imwitor 191,308(1),380,742,780 K,928,988
5	Labrafil M 1944 CS, M 2125 CS
6	Lauroglycol 90
7	PEG MW > 400
8	Plurol oleique CC 497
9	Poloxamer 124 & 188
10	Softigen 701, 767
11	Tagat TO
12	Tween 8

References

1. Tadros T, Izquierdo P, Esquena J, Solans C. Formation and stability of nano-emulsions. Advances in colloid and interface science. 2004 May 20;108:303-318. doi: 10.1016/j.cis.2003.10.023.
2. McClements DJ, Decker EA, Weiss J. Emulsion-based delivery systems for lipophilic bioactive components. Journal of food science. 2007 Oct;72(8):R109-124. doi: 10.1111/j.1750-3841.2007.00507.
3. Garti N, Benichou A. Recent developments in double emulsions for food applications. Food emulsions. 2004;132:353-412. doi: 10.1201/97802039132 22.
4. Weiss J, Takhistov P, McClements DJ. Functional materials in food nanotechnology. Journal of food science. 2006 Nov 1;71(9):R107-116. doi: 10.1111/j.1750- 3841.2006.00195.
5. 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):331-352. doi: 10.1111/1541-4337.12189.
6. Karthik P, Ezhilarasi PN, Anandharamakrishnan C. Challenges associated in stability of food grade nanoemulsions. Critical reviews in food science and nutrition. 2017;57(7):1435-1450.
7. Qian C, McClements DJ. Formation of nanoemulsions stabilized by model food-grade emulsifiers using high-pressure homogenization: Factors affecting particle size. Food hydrocolloids. 2011;25(5):1000-1008.
8. Mu H, Holm R, Müllertz A. Lipid-based formulations for oral administration of poorly water-soluble drugs. International journal of pharmaceutics. 2013;453(1):215-224.
9. Mc Clements DJ. Nanoemulsions versus microemulsions: terminology, differences, and similarities. International Journal of Pharmaceutics. 2012;8:1719-1729.
10. Acosta E. Bioavailability of nanoparticles in nutrient and nutraceutical delivery. Current opinion in colloid & interface science. 2009;14(1):3-15.
11. Čerpnjak K, Zvonar A, Gašperlin M, Vrečer F. Lipid-based systems as promising approach for enhancing the bioavailability of poorly water-soluble drugs. Acta pharmaceutica. 2013;63(4):427-445.
12. Gibaud S, Attivi D. Microemulsions for oral administration and their therapeutic applications. Expert opinion on drug delivery. 2012;9(8):937-951.
13. Rehman FU, Shah KU, Shah SU, Khan IU, Khan GM, Khan A. From nanoemulsions to self-nanoemulsions, with recent advances in self-nanoemulsifying drug delivery systems (SNEDDS). Expert opinion on drug delivery. 2017;14(11):1325-1340.
14. Saifullah M, Ahsan A, Shishir MR. Production, stability and application of micro-and nanoemulsion in food production and the food processing industry. Inemulsions 2016; 405-442). Academic Press.
15. 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.
16. Velikov KP, Pelan E. Colloidal delivery systems for micronutrients and nutraceuticals. Soft matter. 2008;4(10): 1964-1980.
17. Azeredo HM, Mattoso LH, Wood D, Williams TG, Avena-Bustillos RJ, McHugh TH. Nanocomposite edible films from mango puree reinforced with cellulose nanofibers. Journal of food science. 2009;74(5):N31-35.
18. Rojas-Graü MA, Soliva-Fortuny R, Martín-Belloso O. Edible coatings to incorporate active ingredients to fresh-cut fruits: a review. Trends in food science & technology. 2009;20(10):438-447.
19. Salvia-Trujillo, L., Rojas-Graü, M. A., Soliva-Fortuny, R., and Martín- Belloso. Useofantimicrobialnanoemulsionsasedib lecoatings:impactonsafety and quality attributes of fresh-cut Fuji apples. Postharvest Biol. Technol. 2015;105:8-16. doi: 10.1016/j.postharvbio.2015.03.009.
20. Donsì F. Applications of nanoemulsions in foods. InNanoemulsions 2018;349-377. Academic Press. doi: 10.1016/B978-0-12-811838-2.00011-4.
21. Chen L, Remondetto GE, Subirade M. Food protein-based materials as nutraceutical delivery systems. Trends in Food Science & Technology. 2006;17(5):272-283. doi: 10.1016/j.tifs.2005.12.011.
22. Bouchemal K, Briançon S, Perrier E, Fessi H. Nano-emulsion formulation using spontaneous emulsification: solvent, oil and surfactant optimisation. International journal of pharmaceutics. 2004;280(1-2):241-251.
23. Pouton CW, Porter CJ. Formulation of lipid-based delivery systems for oral administration: materials, methods and strategies. Advanced drug delivery reviews. 2008;60(6):625-637.
24. Pouton CW. Lipid formulations for oral administration of drugs: non-emulsifying, self-emulsifying and 'self-microemulsifying'drug delivery systems. European journal of pharmaceutical sciences. 2000 Oct 1;11:S93-S98.

25. Pershing LK, Parry GE, Lambert LD. Disparity of in vitro and in vivo oleic acid-enhanced β-estradiol percutaneous absorption across human skin. Pharmaceutical research. 1993;10(12):1745-1750.
26. Wang Y. Preparation of nano-and microemulsions using phase inversion and emulsion titration methods: a thesis presented in partial fulfilment of the requirements for the degree of Master of Food Technology at Massey University, Auckland, New Zealand (Doctoral dissertation, Massey University) (2014).
27. Hadgraft J. Skin, the final frontier. International Journal of Pharmaceutics, 2001;224:1-18.
28. Shi Y, Li H, Li J, Zhi D, Zhang X, Liu H, Wang H, Li H. Development, optimization and evaluation of emodin loaded nanoemulsion prepared by ultrasonic emulsification. Journal of drug delivery science and technology. 2015;27:46-55.
29. (Bhatt and Madgav, 2011).
30. Singh Y, Meher JG, Raval K, Khan FA, Chaurasia M, Jain NK, Chourasia MK. Nanoemulsion: Concepts, development and applications in drug delivery. Journal of controlled release. 2017;252:28-49.
31. Montserrat, Roca Foguet, (Leverkusen DE) Nanoemulsion. United States Patent Application 20090324727 Assignee: Biofrontera Bioscience Gmbh (Leverkusen, De).
32. Arunkumar N, Deecaraman M, Rani C. Nanosuspension technology and its applications in drug delivery. Asian Journal of Pharmaceutics (AJP): Free full text articles from Asian J Pharm. 2014;3(3).
33. Anton, N., Benoit, J.-P., and Saulnier, P. Design and production of nanoparticles formulated from nano-emulsion templates—a review. J. Control. Release 2008;128, 185–199. doi: 10.1016/j.jconrel.2008.02.007.
34. Shakeel F, Baboota S, Ahuja A, Ali J, Faisal MS, Shafiq S. Stability evaluation of celecoxib nanoemulsion containing Tween 80. Thai J Pharm Sci. 2008;32:4-9.
35. Devarajan V, Ravichandran V. Nanoemulsions: as modified drug delivery tool. Int J Compr Pharm. 2011;2(4):1-6.
36. Shah P, Bhalodia D. Nanoemulsion: A Pharmaceutical Review. Sys Rev Pharm. 2010;1(1):24-32.
37. Baboota S, Shakeel F, Ahuja A, Ali J, Shafiq S. Design, development and evaluation of novel nanoemulsion formulations for transdermal potential of celecoxib. Acta pharmaceutica. 2007 Sep 1;57(3):315.
38. Tiwari SB, Amiji MM. Nanoemulsion formulations for tumor-targeted delivery. InNanotechnology for cancer therapy 2006; 723-739). CRC Press.
39. Simonnet JT, Sonneville O, Legret S, inventors; LOreal SA, assignee. Nanoemulsion based on ethoxylated fatty ethers or on ethoxylated fatty esters and its uses in the cosmetics, dermatological and/or ophthalmological fields. United States patent US 6,375,960. 2002.
40. Valdivia FJ, Dachs AC, Perdiguer NC, inventors; Laboratorios Cusi SA, assignee. Nanoemulsion of the oil water type, useful as an ophthalmic vehicle and process for the preparation thereof. United States patent US 1997;5:698,219. .
41. Banker GS, Lieberman HA, Rieger MM: Pharmaceutical dosage forms. Disperse systems, Marcel Dekker, Edition 2, 2002;3:33940,343-44.
42. Higuchi WI, Misra J. Physical degradation of emulsions via the molecular diffusion route and the possible prevention thereof. Journal of pharmaceutical sciences. 1962;51(5):459-466.
43. Yu H, Huang Q. Improving the oral bioavailability of curcumin using novel organogel-based nanoemulsions. Journal of agricultural and food chemistry. 2012; 60(21):5373-5379.
44. Kemken J, Ziegler A, Müller BW. Influence of supersaturation on the pharmacodynamic effect of bupranolol after dermal administration using microemulsions as vehicle. Pharmaceutical research. 1992;9(4):554-558.
45. Mason TG, Wilking JN. K. meleson, CB Chang and SM Graves. J. Phys.: Condens. Matter. 2006;18:R635.
46. Fryd MM, Mason TG. Advanced nanoemulsions. Annual review of physical chemistry. 2012 May 5;63:493-518.