Chapter

Introductory Chapter: From Microemulsions to Nanoemulsions

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1. Introduction

In the past two decades, there has been much attention within food and beverages, pharmaceutical, biomedical, special chemicals and other industries in using colloidal as main media for process encapsulation, protection and delivery of various active components for different purposes [1–3].

This dispersion normally exists as a suspension of small particles within a liquid medium. Conventionally, particles at >1000 nm are studied due to its rising trend of research interest as a result of introduction of microfluidics [4]. Microfluidics is a concept that is defined as a branch of fluid mechanics that focuses on the understanding, design, fabrication and operation systems that convey liquids and gases inside an enclosed channel with two of the three geometry length scales are in the order of microns (10^{-6}). The reduction in dimension had magnified the effect of some uncommon macroscale liquid properties such as surface tension, capillary effect and material hydrophilicity/hydrophobicity. The first ventures in microfluidic started in the early 1950s when dispersion methods of nano- (10^{-9}) and pico- (10^{-12}) litre of fluids were developed, which served as the foundation of modern day Inkjet technology [5, 6]. As microfluidics' continuous development advanced for the past 70 years, multiple cross disciplines with intersections of engineering, physics, chemistry, biology, nanotechnology and biotechnology had been developed and commercialised. In 2003, Forbes magazine named microfluidics technology as one of the most important inventions that can affect the future of humanity [7]. Meanwhile, microfluidics hold some of the key advantages that include the low manufacturing costs, economic use and disposal, shorter time of analysis, minimal consumption of reagents and samples, minimal production of potentially harmful by-products, enhancement of separation efficiency, enhancement of portability for point-of-care testing, high surface to volume ratio and small laboratory footprint [8, 9].

On the other hand, there are some colloidal applications that desire very much smaller particles (<100 nm) since they have advantages over microscale colloids, such as better stability to particles aggregation and gravitational separation [2], weak light scattering [10–12], and have novel physical properties (i.e., high viscosity and gel-like behaviour) [2, 13]. In conjunction with the new rise of nanotechnology research trend, a decent amount of research has been devoted to fabrication, characterization and application of colloidal dispersion that contains of nanometre-sized particles as delivery systems. As the research duration is merely less than two decades, much knowledge gap in this research field remains to be filled.

This chapter therefore emphasizes the most commonly used terms in this field of study, namely microemulsions (>1000 nm) and nanoemulsions (<100 nm). Using oil-in-water (O/W) system, which is widely used as delivery systems in a range of different industries as well as many literatures, this chapter will outline the similarities and differences between microemulsions and nanoemulsions, to articulate the scientific terminology used to describe each of the terms and also to look into research progress of both microemulsions and nanoemulsions as a whole.

2. Terminology

In this section, some fundamental concepts on similarity as well as difference for both microemulsions and nanoemulsions will be provided, respectively, in terms of its physical and chemical properties, stability and thermodynamic difference as well as the current fabrication methods. These terminologies are meant to clarify the common confusions found in most literatures.

2.1 Physical and chemical properties

2.1.1 Microemulsions

The definition of microemulsions is commonly described as a stable liquid droplet in microscale ($r < 100\ \mu m$) formed by mixing of two immiscible phases, i.e., oil and water in the presence of surfactant. The emulsion's structure, size, composition and surface behaviour can be manipulated by different fabrication methods. They may form one or multiple phases (with different shapes) that are in equilibrium with one another [14]. As for analysis, common analytical equipment such as light-inverted microscopy, scanning electron microscopy, X-ray powder diffraction, electrical conductivity and rheology are usually chosen as tools for the study focus. Therefore, it is advisably to classify microemulsion (O/W) as a thermodynamically stable colloidal dispersion. The structure hinders the unfavourable contact area between non-polar groups and water, which favour the thermodynamics of the colloidal dispersion system. For instance, the surfactant molecules in an oil-in water (O/W) microemulsions has the setup of non-polar tails that associate with each other forming a hydrophobic core. The hydrophilic head groups extrude onto the surrounding aqueous phase of the microemulsion. Meanwhile, the hydrophobic oil molecules may assimilate into the interior of a micelle as a separate core or serves as a barrier between the surfactant tails as shown in **Figure 1**. If oil molecules have the same polar groups, they may then be integrated into the micelle in such a way that it creates a visible distance into the water. This behaviour is particularly important in pharmaceutical industry as it serves as a fundamental core structure for self-microemulsifying drug delivery system. It extends the knowledge for drug delivery system design in terms of the optimum composition of the initial system and the optimum method to dilute the surface of the microemulsion.

2.1.1 Nanoemulsions

Nanoemulsions are considered to be a classic liquid emulsion formation from two immiscible liquids that is thermodynamically unstable. Theoretically, this small spherical droplet ($r < 100$ nm) could be formed using oil (as continuous phase) and water (as dispersed phase) without addition of a surfactant. However, this system will be highly unstable; thus, most nanoemulsions would require the assistance of surfactant (often it is more than one type of surfactants used) to facilitate its droplet formation. The fundamental component formation of a nanoemulsion is very similar to those found in a microemulsion as

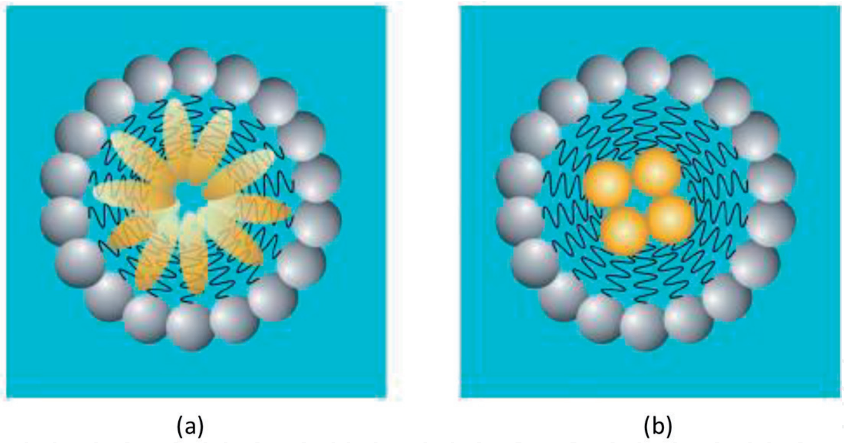

Figure 1.
Oil-in-water microemulsions: (a) oil molecules assimilate between the surfactant tails; and (b) oil molecules incorporated as a hydrophobic core. Reprinted with permission from Ref. [3].

mentioned above. The only distinctive difference that separates a nanoemulsion from a microemulsion is their thermodynamic stability, i.e., a microemulsion is thermodynamically stable while a nanoemulsion is not. As nanoemulsion only has a short development history of ~25 years [15], there are much area of interest that are waiting to be explored with most of the current understanding for Nanaoemulsions is adapted based on Microemulsions understanding. The summary of similarities and differences between microemulsions and nanoemulsions can be seen in **Table 1**.

The chapter so far outlines the similarity and differences between nanoemulsions and microemulsions based on their general physical and chemical properties, as well as other characteristics. In this section, an attempt to propose practical methods to distinguish nanoemulsions from microemulsions will be made. The key concept to make this comparison is based on thermodynamic point of view as shown in **Figure 2** below. As the terms used for microemulsions and nanoemulsions remain confusing in most literatures, the following two factors can be used as a guideline to distinguish nanoemulsions from microemulsions:

2.1.1.1 Long-term storage

Nanoemulsions are not thermodynamically stable, whereas microemulsions are. This simply means microemulsions will not undergo deformation at an infinite period so long the storage condition remains constant. For nanoemulsions, degradation of structure is noticeable due to Ostwald ripening, flocculation, coalescence and gravitational separation. These result in particle size distribution change, physical properties change as well as chemical properties change. Practically, it can be difficult to just make a justification to distinguish nanoemulsions from microemulsion merely based on long-term storage, since microemulsions commonly suffer from chemical degradation and microbial contamination during the storage period.

2.1.1.2 Particle size

As mentioned above, microemulsions have tendency to form single narrow size distribution, ought to its maturity in terms of fabrication methods. Adding to its thermodynamic stability, the size of a microemulsion will not undergo changes once it is formed by a specific approach. This is different from nanoemulsions where they tend to have multiple peaks in its size distribution. This

Descriptions	Microemulsion	Nanoemulsion	Remarks
Size	1 nm (1×10^{-9} m) to 100 nm (1×10^{-6} m)		The difference between microemulsions and nanoemulsions cannot be distinguished merely from size
Particle size distribution	Tend to have single narrow peak for size distribution	Have multiple peaks for size distribution	Normally, the combination of micro- and nanoemulsions exists in multiple peaks colloid distribution
Water-in-oil/oil-in-water formation	Possible		Both microemulsion and nanoemulsion can form water-in-oil and oil-in-water emulsion type
Composition	An oil phase, an aqueous phase, a surfactant and possibly a co-surfactant [1]		A greater surfactant-to-oil ratio is required to prepare a microemulsion than a nanoemulsion due to size difference
Optical properties	Opaque or semi-transparent [3]	Transparent when the size is ≤30 nm [12]	
Thermodynamic stability	Kinetically stable for indefinitely	Unstable system that will break down over time [3]	Microemulsions will not undergo breakdown provided the storing condition remains unchanged Nanoemulsions will breakdown and revert back to separated phase, subject to energy barrier between nanoemulsions and separated phase (Gibbs free energy, ΔG)
Gravitational stability	Not reported	Colloidal dispersion to gravitational separation (creaming/sedimentation) increases significantly for particle size ≤90 nm due to dominance of Brownian motion [3]	Limited work has been to validate this area of research
Particle structure	Spherical or non-spherical, subject to fabrication method used [14]	Spherical	The governing equation is used to determine particle size, thus the structure Laplace pressure, $\left(\Delta P_L = \frac{2\gamma}{r}\right)$. The small radius of nanoemulsions has relative large Laplace pressure, thus sphere sharp has lowest interfacial area
Fabrication methods	Principally, it can form spontaneously due to its thermodynamic stability. In practical, external force will be exerted to emulsion formation	External energy must be applied to overcome positive free Gibbs energy to form emulsion. Common fabrication approaches are high energy, low energy, and phase inversion [3, 16]	Difficult to distinguish based on fabrication methods

Table 1.
Summary of microemulsion and nanoemulsion common facts and common differences.

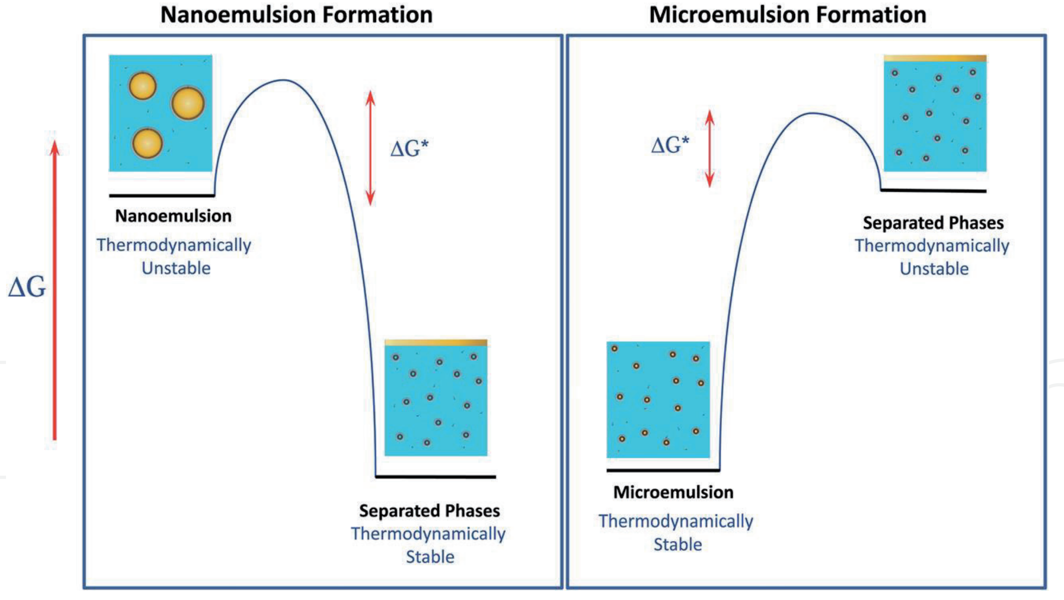

Figure 2.
Schematic illustration between microemulsions and nanoemulsions, with its separated phase state, respectively. Microemulsions have a relative lower free Gibbs energy than the phase-separated state; therefore, it is unlikely to break down even after a long storage period provided the storage condition remains unchanged. Meanwhile, nanoemulsions have a higher free Gibbs energy, leading to breakdown and revert back to its original separated state despite the assistance of surfactants. Reprinted with permission from Ref. [3].

is not surprising due to its unstable thermodynamic as discussed previously. Therefore, if an emulsion system has multiple peaks formation in its size distribution, it can possibly be considered as a system that has both microemulsions and nanoemulsions. However, the noticeable approach to be used in this scenario is to undergo proper physical characterization such as Zetasizer or using scanning electron microscope for proper size measurement, as well as storing it for a period of time, i.e., 1 year to observe the change of emulsion structure. These approaches might provide other significant evidence to validate the type of emulsion formation.

3. Conclusion

This chapter is a timely content of nanoemulsion development as this research field has shown significant publication output for the past decade due to growing interest as a result of nanotechnology development as seen in **Figure 3** using Web of Knowledge (Thomson Reuters) online search engine [15]. Presently, microemulsion-related publication is dominating in terms of publications output per year. This is in line with the history of microemulsion for the past seven decades which covers a comprehensive research range from science (i.e., chemistry, biology, physics, etc.) to engineering (chemical, biomedical, environmental, etc.). On the contrary, nanoemulsions received much lesser focus until the mid-1990s. It has relative incomplete fundamental knowledge understanding in terms of properties, characterizations and fabrication methods, and it also has limited applications presently. Therefore, this book is important in attempting to mend the knowledge gap and form the trend. As nanotechnology matures gradually, the outlook of nanoemulsion looks bright and it aims to stretch its capability to apply across different fields that will benefit mankind.

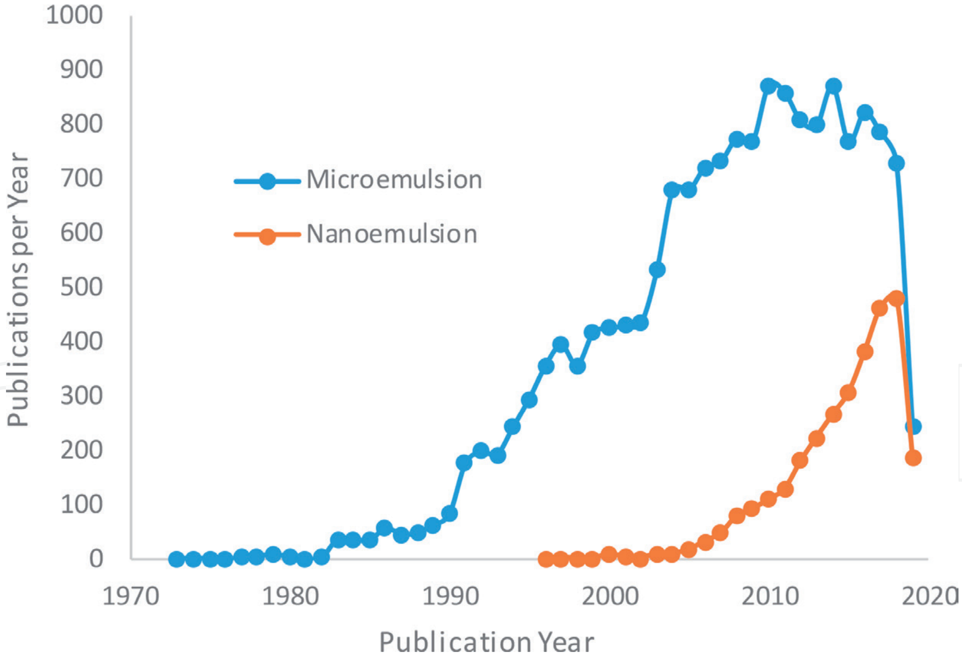

Figure 3.
Comparison between 'microemulsion' and 'nanoemulsion' in terms of publication per year using Web of Knowledge online search engine in May 2019.

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