

Review on Nanoemulsion: Preparation and Evaluation

Zainab A. Sadeq

Department of Pharmaceutics, College of Pharmacy, University of Baghdad, Iraq

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ABSTRACT

Nanoemulsion considers a novel drug delivery system that permits controlled or sustained drug release. It is a dispersion consisting of a surfactant, oil, and clear aqueous phase, kinetically, or thermodynamically stable with droplet diameter 10-100nm. Nanoemulsion applied to increase the solubility and bioavailability of lipophilic drugs; they have many advantages for drug delivery. There are many methods for Nanoemulsion preparation like High –energy emulsification method, Spontaneous Nanoemulsion, Phase inversion temperature (PIT). It applied for many routes of delivery, thus providing a promising effect for many fields such as cosmetics, therapeutic, and biotechnology.

Keywords: Application, Methods of preparation, Nanoemulsion, Surfactant.

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INTRODUCTION

Nanoemulsion preparation is an advance delivery system used for drugs, biologically active, and genetic substances that have release problems .since 40% of chemical substances are naturally water-insoluble, and the delivery of these hydrophobic substances is a challenge for there delivery. Nanoemulsion can be defined as a colloidal dispersion consists of an appropriate ratio of oil emulsified in the aqueous phase, surfactant, and co-surfactant. Nanoemulsion is clear, thermodynamic, and kinetic stability. It used in pharmaceutical industries because it increases the solubility of lipophilic drugs that lead to bioavailability improvement of these substances by particle size reduction of powdered drugs and nano-sized droplet formation with range(10-100 nm).¹ There are differences between emulsion and nanoemulsion that are emulsion exhibit good kinetic stability, unstable thermodynamically, and cloudy while nanoemulsion is translucent or clear. Also, in an emulsion, preparation required a large input of energy while in Nanoemulsion do not require energy input.²

Advantage of Nanoemulsion⁴

- Decrease the absorption variability
- Enhancing the solubility of lipophilic substances
- Use to mask the unpleasant taste
- Use for drug delivery through different routes like i.v, oral, and topical.
- Provided efficient and rapid penetration of the drug through the skin and GIT.

Disadvantage of Nanoemulsion⁵

- It required the use of surfactant and co-surfactant in large concentrations that are essential for stability.
- Stability of Nanoemulsion affected by environmental factors like pH and temperature.
- Surfactant and co-surfactant used should be nontoxic.
- Low solubility capacity for high melting materials.

Nanoemulsion types⁶

Depending on the oil and water phase of Nanoemulsion, it is classified into three types:

- Oil in water (o/w) Nanoemulsion, in this system, oil droplet of internal phase dispersed in the external aqueous phase.

Table 1: Difference between Emulsion, Nanoemulsion, and microemulsion³

Emulsion	Nanoemulsion	Microemulsion
Excellent kinetic stability	Kinetically unstable	Possess some kinetic stability
Thermodynamically unstable and will eventually phase separate	Thermodynamically stable and no phase separation	Thermodynamically stable
Emulsion appear cloudy	Nanoemulsion are clear or translucent	microemulsion are clear
Method of preparation requires a large input of energy	Method of preparation doesn't require a large input of energy	Method of preparation doesn't require a large input of energy

- Water in oil (w/o) Nanoemulsion, in this system, water droplet of internal phase dispersed in the external oil phase.
- Bi-continuous Nanoemulsion in this system, both oil and water droplets are interspersed through the system.

The stability of these three types of Nanoemulsion obtained by adding sufficient compatible surfactant and co-surfactant to reduce the interfacial tension, the surfactant could be anionic, cationic, and nonionic.

Component of Nanoemulsion

- Oil
- Surfactant
- Co- Surfactant
- Aqueous phase

Oil

The oil selection used in Nanoemulsion formulation considers as an important factor since the drug will be incorporated as a droplet in the oily phase that dispersed in the aqueous phase. So, the oil which is selected should able to dissolve the substances used in dosage form to get a higher % of drug-loaded, also oil selected must be compatible with other Nanoemulsion component. The oil used in Nanoemulsion either natural, synthetic, or semi-synthetic.⁸

Surfactant (surface-active agent)

Surfactants are substances that decrease interfacial tension or surface tension occurring between a solid and a liquid. Surfactant act either as an emulsifier, wetting agent, foaming agent, detergents, and dispersants, which depending on hydrophilic-lipophilic balance (HLB) value. The use of surfactant in preparation of Nanoemulsion to stabilize the system and chooses it to depend on Nanoemulsion type to be prepared Hydrophilic Surfactant with HLB value more than 10 used for o/w nanoemulsion, while hydrophobic Surfactant with HLB value less than 10 used for w/o Nanoemulsion. The use of Surfactant combinations with low and high HLB value leading to the formation of good stability Nanoemulsion upon water dilution.⁹

Co- Surfactant

These materials added to Nanoemulsion formulation to decrease the interfacial tension that occurs between oil and water when the surfactant failed to decrease it. In addition, it provided some fluidity to the interfacial tension of Surfactant when it has high rigidity, through penetrating into a monolayer of surfactant and disrupting its crystalline liquid phase, an example of Co-Surfactant propylene glycol, poly glyceryl oleate, PEG 400.¹¹

Aqueous phase

Deionized water used in Nanoemulsion formulation as an aqueous phase since its pH 7 and has no electrolytes. The stability of Nanoemulsion and its droplet size influenced by the nature of aqueous phases like ionic content, electrolytes, and pH. The electrolyte decreases the repulsion force between droplet due to zeta potential reduction and pH changing of formulation leading droplet flocculation in the formulation.¹²

Methods of Nanoemulsion preparation

High-energy emulsification method

Nanoemulsion considers as a non-equilibrium system since it cannot spontaneously formed so that chemical or mechanical energy input is required to formulate it. Nanoemulsion prepared by High-energy method through utilizing mechanical energy input by using ultrasound generator, high-pressure homogenizers, and high shear stirring.¹³ These mechanical devices support strong forces that make oil and water phase disruptions to form Nanoemulsion. In high pressure, homogenizers supplied with energy in the shortest time in order to produce homogeneously small-sized droplets so that it widely used in Nanoemulsion preparation. While an ultrasound generator is cost-effective since needing less surfactant.¹⁴

Low-energy emulsification method

This method provided more uniformly and smaller droplets through using physicochemical characterize of the system.¹⁵ There is some limitation for this method about using some oil and emulsifier types such as polysaccharides and proteins. To solve this problem, synthetic surfactants at high concentrations are used with techniques at low energy, but this is narrowing its application space, especially for food processing.¹⁶

Spontaneous Nanoemulsion

It utilizes the chemical energy released upon processes of dilution with a continuous phase, which happens at a constant temperature throughout the emulsifications procedure, without any phase transition in the system.¹⁷ This method produces Nanoemulsion without special device at room temperature. In this system, an oil phase with a hydrophilic substance mixed with water, oil droplet immediately formed, this mechanism depends on water-dispersible material movement from oil to water phase as red arrows which lead to spontaneous oil droplet formation.¹⁶

Table 2: Surfactant property according to HLB value¹⁰

HLB value	Surfactant Property
(0-3)	Anti-foaming agent
(4-6)	Water in oil (W/O)emulsifier
(7-9)	Wetting agent
(8-18))	Oil in water(O/W) emulsifier
(13-15)	detergents
(> 15)	Solubilizing agent

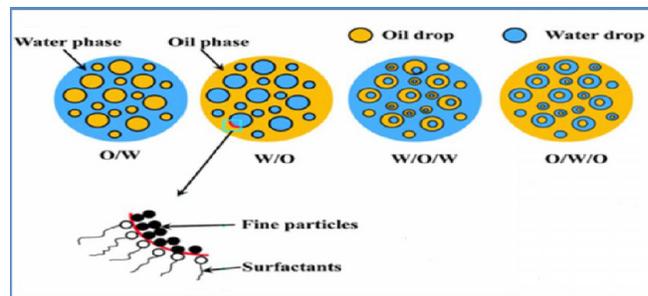


Figure 1: The types of Nanoemulsion⁷

Phase inversion temperature (PIT)

In this method, there is changing in temperature with a constant composition. Nonionic surfactants like poly ethoxylated have temperature depended on solubility. Therefore, those emulsifications occurred by modifying surfactant affinities to oil and water as a function of temperature. In the PIT method, the interfacial tension and droplet size reach the smallest value; this method produces emulsifications by utilizing the low interfacial tension at HLB temperature.¹⁸

Phase inversion composition (PIC)

In this method, there is changing in composition temperature at a constant temperature. The (PIC) method used for a large scales production than (PIT) because the addition of a single component to the emulsion is easier than producing a change in temperature. Nanoemulsion produced by consistent addition of oil or water to water –surfactant or oil-surfactant mixture.¹⁷

Applications of Nanoemulsion^{10,19,20,21}*Nanoemulsion for oral route*

The poorly water-soluble drugs have low bioavailability because they have a low rate of dissolution; therefore o/w Nanoemulsion for these drugs lead to increase its solubility, absorption, and bioavailability after oral administration

Nanoemulsion for ocular delivery

For improvement, lipophilic drugs delivery to the eye, o/w Nanoemulsion used such as pilocarpine, erythromycin.

Nanoemulsion for nasal delivery

The nasal route possesses many advantage comparing with the perioral and parenteral route, such as by pass first metabolism in the liver, increasing the contact time between nasal mucosa and Nanoemulsion droplet leading to increase drug absorption.

Nanoemulsion for transdermal delivery

The chemical substance can penetrate the skin layer by three ways that are hair follicles, sweat duct or directly through stratum corneum that restrict drug absorption and decrease its bioavailability. To improve drug targeting and to control drug redistribution throughout blood and lymph vessels. Nano-sized emulsion has abilities to penetrate the skin pores and reaching the systemic delivery; also Nanoemulsion considers a promising technique with advantage like low cost of preparation, high stability during storage, no organic solvent and thermodynamics stable.

Nanoemulsion in cosmetic

Nanoemulsion considers as good vehicles for controlled cosmetic delivery and facilitates the dispersion of active substances in the skin layer. Nanoemulsion used in cosmetics because no sedimentation, creaming, flocculation that happen with microemulsion.

CONCLUSION

Nanoemulsion used for many applications in pharmacies such as drug delivery systems since their abilities of solubilizing water-insoluble substances. Nanoemulsion possesses many

advantages of the delivery drug, diagnostic, and biological substances. Also, it is a protected labile drug, increasing drug solubility, and bioavailability.

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