IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

REVIEW ON "PREPARATION AND EVALUATION OF NANO EMULSION"

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Abstract
Nano emulsion is a novel drug delivery system that controlled or sustained drug release. It is a dispersion with a droplet diameter of 10-100 nm that is made up of an oil, surfactant, and clear aqueous phase. It is stable either thermodynamically or kinetically. Lipophilic pharmaceuticals are given a Nano emulsion application to improve their solubility and bioavailability; these solutions have numerous benefits for medication delivery. There are numerous techniques for Nano emulsion preparation such High –energy emulsification method, Spontaneous Nano emulsion, Phase inversion temperature (PIT). It has applications in numerous delivery methods, showing promise in a variety of industries, including biotechnology, medicine, and cosmetics.

Keywords: Nano emulsions, Surfactant, Water in Oil (W/O), Oil in Water (O/W), Application, and Method of Preparation.

Introduction

One innovative medicine delivery method is nanoemulsion. It is one of the cutting-edge methods for improving the bioavailability of medications that are not highly soluble in water [1]. Nano emulsions are submicron sized colloidal particle systems; they are also referred to as submicron emulsions, ultrafine emulsions, and miniemulsions [2]. Numerous industries, including the culinary, pharmaceutical, cosmetic, and agricultural sectors, are seeing rapid growth in nanotechnology [3]. As a cutting-edge drug delivery technique, Nano emulsions (NE) reduce side effects and harmful responses while maximizing the pharmacological and therapeutic activity of pharmaceuticals [4]. In addition to the lipid and aqueous phases, stabilizers like emulsifiers and hydrocolloids are needed in the formulation of Nano emulsions to stop the Nano emulsion structure from disintegrating after it has formed. Enzymes have surface activity. amphiphilic compounds have polar media affinity for the hydrophilic portion and non-polar media affinity for the lipophilic half. During emulsification, they have the ability to adsorb at the oil–water interface of droplet surfaces, shielding the droplets from aggregation or re-coalescence. [5] Are focused on creating lipophilic materials such as pharmaceuticals, fatty acids, colours, and favours. [6] When two immiscible liquids are mixed with an emulsifier, stable yet kinetic dispersions with droplet sizes and diameters of less than 100 nm and 20–200 nm, respectively, are created. These dispersions are known as Nano emulsions. When the Brownian motion of the nanoparticles outpaces the gravitational forces of the emulsions, the particles become kinetically stable and cease to aggregate. [7]

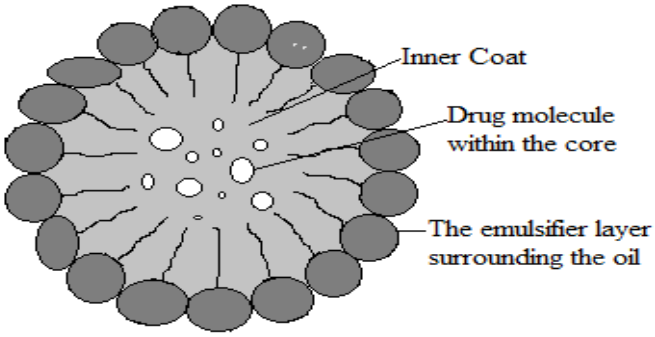

Figure 1: Structure of Nano emulsion

Advantage of Nano emulsion

1. Reduce the unpredictability of absorption
2. Improving lipophilic compounds' solubility
3. Use to cover up the bad flavour.
4. Use for topical, oral, and IV medication administration, among other routes.
5. facilitated quick and effective medication absorption via the skin and GIT [8]

Disadvantage of Nano emulsion

1. It required the use of surfactant and co-surfactant in large concentrations that are essential for stability.
2. Stability of Nano emulsion affected by environmental factors like pH and temperature.
3. Surfactant and co-surfactant used should be nontoxic.
4. Low solubility capacity for high melting materials.[9]

Nano emulsion types

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

1. **Oil in water (o/w) Nano emulsion**: In this system, oil droplet of internal phase dispersed in the external aqueous phase.[10]
2. **Water in oil (w/o) Nano emulsion**: In this system, water droplet of internal phase dispersed in the external oil phase.
3. **Bi-continuous Nanoemulsion** There are water and oil droplets scattered throughout this system. These three forms of nanoemulsions are stable when a suitable amount of surfactant and co-surfactant is added to lower the interfacial tension. Anionic, cationic, and nonionic surfactants can all be used.[11]

Table

Emulsion	Droplet Size	Thermodynamic Stability	Stability
Macroemulsion	0.1-100 µm	Unstable	Turbid
Microemulsion	5-100 nm	Stable	Transparent
Nanoemulsion	5-200 nm	Unstable	Transparent

Nanotechnology is developing rapidly in many sectors, especially cosmetics, pharmaceutics, agriculture and food industries. [12]

Component of Nanoemulsion

1. Oil
2. Surfactant
3. Co- Surfactant
4. Aqueous phase

1. **Oil - Droplets** of both water and oil are dispersed throughout this system. By adding enough suitable surfactant and co-surfactant to lower the interfacial tension, these three forms of nanoemulsions become stable. The surfactant can be nonionic, cationic, or anionic. [13]
2. **Surfactant (surface-active agent)** - Surfactants are compounds that reduce surface tension or interfacial tension that exists between a liquid and a solid. Depending on the hydrophilic-lipophilic balance (HLB) ratio, surfactants can function as emulsifiers, wetting agents, foaming agents, detergents, or dispersants. Surfactant is used in the preparation of nanoemulsion to stabilize the system; the type of surfactant used depends on the type of nanoemulsion being generated. For o/w nanoemulsion, hydrophilic surfactants with an HLB value greater than 10 are utilized, whereas hydrophobic surfactants with an HLB value less than 10 are utilized for w/o nanoemulsions. Combinations of surfactants with low and high HLB values are used to create good stability. After diluting water, a nanoemulsion. [14]

3. **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.[15]
4.
5. **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 [16].

Methods of Nanoemulsion preparation

1. **High pressure homogenization:**

Nanoemulsion preparation required high shear force, therefore in this strategy high-pressure homogenizer or piston homogenizer is utilized for production of nanoemulsions with very small particle size (up to 1 nm). In this technique, a mixture is forced to pass through an orifice at a very high pressure ranging from 500 to 5000 psi. The resultant product is further subjected to intense turbulence and hydraulic shear resulting into emulsion with extremely fine particles. This has been proved to be the most efficient method for nanoemulsion preparation but the only drawback associated with this technique is high energy consumption and rise in temperature of emulsion during processing. For obtaining smaller particle size, it also requires larger runs of homogenization cycles. Yilmaz et al. formulated phytosphingosine O/W nanoemulsions by employing high pressure homogenization method and found out that droplet size was decreased after 8 homogenisation cycles and such nanoemulsion was stable for over 6 mo. [17]

2. **Micro fluidization:**

This method employed a device known as microfluidizer that utilizes high pressure positive displacement pump (500-20 000 psi) that pushes the product out through the interaction chamber consisting of stainless steel microchannels on the impingement area resulting into formation of very small particles of sub-micron range. The mixture is repeatedly circulated through the microfluidizer until the required particle size is achieved. Resultant product is also passed through the filter to separate smaller droplets from larger ones and to obtain a uniform nanoemulsion. Uluata et al. fabricated octadecane O/W nanoemulsions using a microfluidizer and observed that on increasing the number of passes and homogenization pressure, the droplet size decreased [18]. Goh et al. prepared tocotrienol-rich fraction nanoemulsions by two step homogenization where a primary coarse emulsion was prepared by using a stirrer, which was further processed using a microfluidizer. They reported that the droplets ize reduced from 120 to 65.1 nm after passing through 10 homogenization cycles at an increased pressure [19]

3. **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, and this mechanism depends on water-dispersible material movement from oil to water phase as red arrows which lead to spontaneous oil droplet formation.[20]

4. **Low–energy emulsification method**

This method provided more uniformly and smaller droplets through using physicochemical characterize of the system. 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. [21]

Applications of Nanoemulsion [22, 23, 24, 25]

1. **Nanoemulsion for oral route**

Because poorly water-soluble medicines dissolve slowly, they have limited bioavailability; consequently, oral administration of these drugs via o/w nanoemulsion increases their solubility, absorption, and bioavailability.

2. **Nanoemulsion for ocular delivery**

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

3. **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.

4. **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 stabile.

5. **Nanoemulsion in cosmetic** Nanoemulsion considers as good vehicles for controlled cosmetic delivery and fa7bcilitates the dispersion of active substances in the skin layer. Nanoemulsion used in cosmetics because no sedimentation, creaming, flocculation that happen with microemulsion

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