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An overview on Nanoemulsion Drug Delivery Systems

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Abstract

The nanoemulsion, with droplet sizes ranging from submicron to micron, is one of the most effective dispersed nanosystems. Thermodynamically stable transparent or translucent dispersions of oil and water known as nanoemulsions, sub-micron emulsions (SMEs), and mini-emulsions are held together by an interfacial coating of surfactant and cosurfactant molecules with a droplet size of less than 100 nm.. These appear to be ultrafine dispersions with variable levels of drug loading, viscoelastic properties, and aesthetic characteristics that can be used for a variety of purposes, including drug administration. To create the nanoemulsions, a variety of methods will be used, including solvent evaporation, high pressure homogenization, low energy emulsification, and micro fluidization.

Keywords: Nanoemulsion applications, Nanoemulsion Formation theory, Nanoemulsions preparation

Introduction

A colloidal particle system in the submicron size range known as a nanoemulsion serves as a vehicle for medicinal molecules. They range from 10 to 1,000 nm in size. These carriers are solid spheres with an amorphous, lipophilic, negative-charged surface. The use of magnetic nanoparticles can improve site specificity. They improve the therapeutic effectiveness of the medicine as a drug delivery mechanism and reduce side effects and hazardous reactions. Major uses include the treatment of reticuloendothelial system (RES) infections, liver enzyme replacement therapy, cancer treatment, and immunisation. In a biphasic system known as an emulsion, one phase is deeply distributed in the other phase as tiny droplets with diameters ranging from 0.1 to 100 nm. The inclusion of an emulsifying agent can stabilise the thermodynamically unstable system (emulgent or emulsifier). While the outer phase is referred to as the dispersion medium, external phase, or continuous phase, the dispersed phase is also known as the interior phase or the discontinuous phase. The emulsifying substance is also referred to as an interphase or an intermediate. A "miniemulsion" is a fine oil/water or water/oil dispersion stabilised by an interfacial coating of surfactant molecules with droplet sizes ranging from 20 to 600 nm, and is also referred to as a "nanoemulsion." The transparency of nanoemulsions is due to their small size.

Three different kinds of nanoemulsions can be created:

a) A nanoemulsion of oil in water where the oil is spread in the permanent aqueous phase,
b) The water in the oil nanoemulsion, which contains water droplets continuous oil phase with dispersion, and
c) Bicylindrical nanoemulsions

Theory of Nanoemulsion Formation

Nanoemulsion, which falls under the category of multiphase colloidal dispersion, is primarily distinguished by its stability and clarity. To get high shear, which is typically obtained by using microfluidics or ultrasonic technology, the droplet size is typically reduced to the nanoscale. The names nanoemulsion and microemulsion, commonly referred to as micellar phase or mesophase, have a slight distinction. While the droplets in a nanoemulsion must be ruptured by external shear, the droplets in a microemulsion typically form through thermodynamic self assembly. They are created via a self-assembling equation phase in which surface tension has little effect. The formulation of the Nanoemulsions emphasises the fundamental idea. They typically consist of two immiscible phases, with the addition of a surfactant reducing the interfacial tension between them[1].

Preparation Methods for Nanoemulsions

The best way to create nanoemulsions, which have very small particle sizes, is with high-pressure machinery. High-pressure homogenization and microfluidization are the techniques that are most frequently employed to create nanoemulsions on both a laboratory and an industrial scale. The creation of nanoemulsions can also be accomplished using other techniques including ultrasonification and in-situ emulsification[2].

1. Using High Pressure to Homogenize

High-pressure is needed for nanoemulsion preparation homogenization. This method utilises high-pressure producing nanoemulsions of using a homogenizer or piston homogenizer very small particle size (up to 1nm). By applying extreme pressure to a small inlet aperture, two liquids (oily phase and aqueous phase) are forced through it to become dispersed (500 to 5000 pressure), which subject the product to strong hydraulic stress and turbulence, producing incredibly small emulsion particles. A monomolecular coating of phospholipids surrounds the liquid, lipophilic core of the produced particles, which is segregated from the surrounding aqueous phase. The only drawbacks of this method are its high energy consumption and processing-related emulsion temperature increases[3].

2. Homogenization Pressure's Effect

The process parameter, which ranges from 100 to 150 bars, has been optimised. The obtained particle size, for example, RMRP 22, decreases with increasing size.

3. Homogenization cycles count

The resulting particle size decreases with increasing homogenization cycles. Three, four, or ten cycles are used to complete the cycles. Using the drug's poly disparity index, the number of cycles is examined a cycle, following each.

Advantages

- Scale-up is simple, and batch variance is minimal.
- Small range of sizes for the drug's nanoparticles.
- Ability to be flexible when handling medicine quality.
- Utilised successfully for thermolabile compounds.

4. Microfluidization

A tool called a micro-fluidizer is used in the mixing method known as micro-fluidization. The product is forced into the interaction chamber, which is made up of tiny channels termed "micro-channels," using a high-pressure positive displacement pump (500 to 20000 psi). The product runs through the microchannels and onto the impingement area, producing submicron-sized, extremely small particles. A coarse emulsion is produced by combining the two solutions (the aqueous phase and the oily phase) and processing them in an inline homogenizer. In a micro-fluidizer, the coarse emulsion is further treated to create a stable nanoemulsion. The interaction chamber micro-fluidizer is used to repeatedly feed the coarse emulsion through until the appropriate particle size is achieved. After the big droplets are removed from the bulk emulsion using a filter under nitrogen, a homogenous nanoemulsion is produced.[4]

5. Ultrasonication

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Several research studies that attempt to use the ultrasonic sound frequency for the decrease of droplet size report on the preparation of nanoemulsion. Utilizing a constant amplitude sonotrode at system pressures higher than ambient pressure is an alternative method. It is commonly known that raising the external pressure lowers the ultrasonic field's cavitation threshold, leading to fewer cavitations. Bubbles appear. However, raising the external pressure also raises the cavitation bubbles' collapse pressure. This indicates that when cavitation occurs, the collapse of the bubbles is stronger and more severe than when the pressure is at atmospheric levels. These variations in the navigational intensity can be directly linked to variations in the power density since cavitation is the most significant source of power loss in a low-frequency ultrasonic system. In order to maintain the temperature at the ideal level, the system additionally uses a water jacket.[5]

6. Method of Phase Inversion

This technique uses chemical energy from phase transitions brought on by the emulsification pathway to achieve fine dispersion. When the emulsion's composition is changed while the temperature is held constant, or vice versa, a phase transition results. It was established that an increase in temperature produces chemical changes in polyoxyethelene surfactants due to polymer chain breakdown with temperature when the phase inversion temperature was first determined.[6]

7. Emulsification That Occurs Suddenly [7]

There are three main steps :

1. Creation of a uniform organic solution consisting of a water-miscible solvent with an oil and a lipophilic surfactant, and water-loving surfactant.
2. The aqueous phase received an injection of the organic phase under the formation of the o/w emulsion used magnetic stirring.
3. By evaporation, the water-miscible solvent was eliminated with less pressure.

8. Technique for Solvent Evaporation

This method entails making a drug solution, then emulsifying it in a different liquid that isn't a solvent for the drug. is drug. The solvent evaporates, causing the precipitation of is drug. Both crystal development and particle aggregation can regulated by applying a high-speed to produce large shear forces stirrer [8].

9. Hydrogel Method

It is comparable to the procedure of solvent evaporation. The fact that the drug solvent and drug anti-solvent are miscible is the only distinction between the two techniques. More shear force inhibits Ostwald ripening and crystal development

Aspects of Formulation and Preparation Methods for Nanoemulsion

Nanoemulsion formulation combines an active substance and an additive emulsifier, and. Two of the different ways to make nanoemulsions are high-energy emulsification and low-energy emulsification. High-energy stirring, ultrasonic emulsification, high-pressure homogenization, micro-fluidization, and membrane emulsification are all components of the high-energy emulsification process[9].(Phase inversion temperature, emulsion inversion point, and spontaneous emulsification are components of the low-energy emulsification technique [10,11]. Reverse nanoemulsion can be created in a very viscous solution using a combination technique that combines high-energy and low-energy emulsification.

Components of Nanoemulsion

Oil, emulsifying agents, and aqueous phases are the three primary elements of a nanoemulsion [12,13]. There are many different kinds of oils, including castor oil, corn oil, coconut oil, evening primrose oil, Mineral oil, olive oil, peanut oil, linseed oil, etc. Using water and oil together can create a transient, crude emulsion. Which, upon standing, will divide into two distinct phases as a result of the globules' dispersion coalescing. Such systems can gain stability via emulsifiers or emulsifying agents.

Emulgents are generally seen of as surfactants, similar to spans and tweens, finely divided hydrophilic colloids like acacia split solids, such as veegum and

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bentonite. an emulsifier in along with its emulsifying abilities, it ought to be nontoxic and it should have a good flavour, smell, and chemical stability suitable for the product.

An emulgent has a number of desirable qualities, including:
(1) It need should be able to decrease lowering the surface tension to less than 10 dynes/cm
2) To prevent coalescence, it must be quickly adsorbed around the dispersed phase globule to produce a complete and coherent film,
(3) Its hould help in building up a sufficient zeta potential and viscosity in the system to bring about the most stability
(4) It ought to work at relatively low concentrations. Emulgents create particulate, multimolecular, or monomolecular films surrounding the globules scattered.

Monomolecular Films

By creating a monolayer of adsorbed molecules or ions at the interface and lowering interfacial tension, an emulgent of the surfactant type stabilises a nanoemulsion. Combinations of emulgents are preferred to single emulgents in conte mporary practise. The mixture creates a complicated film at the interface by combining an emulgent that is mostly hydrophilic in the aqueous phase with a hydrophobic agent in the oily phase.

Multimolecular Films

Globules of scattered oil are encircled by multimolecular films made of hydrated lyophilic colloids. Hydrated colloids can create robust, coherent multimolecular films while not significantly decreasing surface tension. The stability of an emulsion is improved by their propensity to make the continuous phase more viscous.

Solid Particulate Films

Small solid particles that are somewhat moistened by both aqueous and non-aqueous liquid phases are the emulgents that create particulate films. As they are concentrated at the interface, a film is created around the scattered globules to stop them from coalescing.

Table no.1.Formulation Ingredients of Nanoemulsion

Components	Examples
Oils	Castor oil, Corn oil, Coconut oil, Evening primrose oil, linseed oil, Mineral oil, olive oil, peanut oil
Emulgent	Natural lecithins from plant or animal source, phospholipids, castor oil. Derivatives, polysorbates, sterylamine
Surfactant	Polysorbate20, Polysorbate80, Polyoxy-60, castor oil, Sorbitan mono oleate, PEG300, Caprylic glyceride
Co- Surfactant	Ethanol, glycerine, PEG300, PEG400, Polyene glycol, Poloxamer
Tonicity modifiers	Glycerol, Sorbitol and xylitol
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 and tocopherol

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Table no.2.List of Oils used in Nanoemulsion

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

Nanoemulsion Applications

Parenteral Delivery

Due to the stringent requirements of this mode of administration, specifically the requirement for the formulation droplet size lower than 1 micrometre, nanoemulsion are advantageous for intravenous administration. Using an injectable or parenteral route, Nanoemulsion is used for many things, including nourishment, for instance. Vitamins, fats, carbohydrates, etc. [14-18]

Lipid nanoemulsions have been extensively researched for parenteral drug administration. Soyabean, sesame, and olive oil nanoemulsions with the non-toxic surfactant pluronic F68 are used for parenteral feeding. When administered parenterally, nanoemulsion formulations offer significant advantages over macroemulsion systems because the fine particle nanoemulsion clears more slowly than the coarse particle emulsion and stays in the body for a longer period of time. O/W as well a parenteral administration can use W/O Nanoemulsion 15th delivery.

Oral Delivery

For oral administration, nanoemulsion formulations have various advantages over traditional oral formulations, including improved clinical potency, increased absorption, and reduced drug toxicity. Therefore, it has been suggested that nanoemulsion is the best delivery system for medications like steroids, hormones, diuretics, and antibiotics. prescription medicines for Proteins and peptides are extremely powerful and Particular to their physiological processes [19].

Primaquine displayed efficient antimalarial action against Plasmodium berghei infection in mice when included in an oral lipid nanoemulsion at a dosage level 25% lower than the standard oral dose. Primaquine's oral bioavailability through the liver was enhanced by lipid nanoemulsion, with drug concentrations at least 45% greater than with the original drug [20].

Topical Delivery

One advantage of topical medication administration over other approaches is the avoidance of the drug's hepatic first pass metabolism and associated adverse consequences. Another is the drug's capacity to target and transport itself directly to the skin or eyes that are being affected. Only systemic antibiotics have been able to attain the same level of topical antibacterial activity as the nanoemulsion. With regard to microorganisms (such as E. coli and S. aureus), the nanoemulsion has extensive antibacterial and antifungal action [21] .

Ocular Delivery

The majority of drug delivery for the treatment of eye disorders occurs topically. For ocular delivery, O/W nanoemulsions have been researched to dissolve poorly soluble medications, boost absorption, and provide a sustained release profile [22,23].

The Cosmetic

Nanoemulsions with droplet sizes under 200 nm and their high surface area, which enables efficient delivery of the active ingredient to the skin, are particularly desirable for use in cosmetics due to their aesthetic features, which include low viscosity and transparent visual aspects. Because macroemulsions exhibit creaming, sedimentation, flocculation, and coalescence, nanoemulsions are suitable for use in cosmetics. Using high-energy machinery throughout manufacture can help you avoid adding any possibly irritating surfactants. Minimizing transepidermal water loss, improving skin protection, and increasing the penetration of active ingredients are all benefits of using nanogel technology to make miniemulsion from oil-in-water concentration. It might be helpful for anti-aging, moisturising, and sun care products. Giving skin care products a proper skin tone helps feelings [24].

Transdermal

In rats with carrageenan-induced paw edoema, indomethacin, a strong NSAID, and the anti-inflammatory effects of a real optimised nanoemulsion formulation were compared with those of commercial gel. The created nanoemulsion's inhibitory value was substantial, indicating tremendous potential for indomethacin transdermal use. Celecoxib was delivered transdermally using nanoemulsions, which contained 2% of the drug, 10% of an oil phase (Sefsol 218 and Triacetin), 50% of a surfactant mixture (Tween 80 and Transcutol-P), and 40% of water. The anti-inflammatory effect and percent inhibition value after 24h administration was found to be high for nanoemulsion formulation (81.2%) as compared to celecoxib gel (43.7%) and nanoemulsion gel (64.5%). The *in vitro- in vivo* studies revealed a significant increase in the anti-inflammatory effects of aceclofenac nanoemulsion (82.2%) as compared to nanoemulsion gel formulation (71.4%) and conventional gel (41.8%) [25,26]

In Biotechnology

In pure organic or aqua-organic conditions, numerous enzymatic and biocatalytic processes take place. These kinds of reactions also employ biphasic media. Biocatalysts become denaturized when pure apolar media are used. The usage of water-resistant media is generally beneficial [26].

Enzymes in low water content display and have:

- A rise in solubility in non-polar reactants.
- Changes in thermodynamic equilibrium that would favour condensations
- Increasing the thermal stability of the enzymes, allowing for higher temperature reactions [27,28].

Conclusion

The most efficient dispersed nanosystem is the nanoemulsion, which has droplet sizes between submicron and micron. Nanoemulsions, sub-micron emulsions (SMEs), and mini-emulsions are transparent or translucent thermodynamically stable dispersions of oil and water held together by an interfacial coating of surfactant and cosurfactant molecules with a droplet size of less than 100 nm. The various methodologies and nanoemulsion used in these review articles.

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