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Literature Review on Nano Emulsion

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Nivetha.M*[1], Karthick.M[1], Divyaparvathi. R[1], Manivannan.R[2], Bagathsingh.C[3], Deivasundari.P[3], Nagarajan.V[3], Srinivas.P[3], Surendharan.P[3]

[1]Assistant Professor, [2] Professor & Principal, [3]B.Pharm Final Year Student

[1, 2, 3] Department of Pharmaceutics, Excel College of Pharmacy, Komarapalayam, Namakkal -637303, Tamilnadu, India.

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ABSTRACT

Nanoemulsions are really one of the most widely used formulation techniques. Nanoemulsions are kinetically stable colloidal systems with microscopic droplet sizes. These are the isotropic systems that are thermodynamically stable when two immiscible liquids are combined to produce a single phase with the proper cosurfactant and surfactant. The diameters of nanoemulsion droplets typically range from 20 to 200 nm. The size and surface characteristics of the Nanoemulsion droplets have a significant impact on how the formulation behaves biologically. For the future of cosmetics, diagnostics, drug therapies, and biotechnologies, nanoemulsion holds out a lot of promise. Thus, the focus of this study is on nanoemulsion types, benefits, drawbacks, formulation features, formulation factors, techniques for characterisation of nanoemulsions and applications.

INTRODUCTION

The terms Mini emulsions, ultrafine emulsions, and submicron emulsions are also used to describe nanoemulsions. The size of the droplets is determined by the surfactant phase structure (bicontinuous microemulsion or lamellar) at the inversion point caused by either temperature or composition, according to phase behaviour studies. Independent of whether the initial phase equilibrium is single or multiphase, studies on the generation of nanoemulsions by the phase inversion temperature method have been demonstrated a link between the smallest droplet size and total oil solubilization in a microemulsion bicontinuous phase.[1]

A variety of surfactants with varying properties (ionic or non-ionic) had been utilised with such nanoemulsions. They were mostly utilised as cationic (quaternary ammonium halide), anionic (potassium laurate, sodium lauryl sulphate), zwitterions (quaternary ammonium halide), and nonionic (sorbitan esters, polysorbates) surfactants. Early nanoemulsions were of the oil-in-water (O/W) type, with droplet sizes averaging between 50 and 1000 nm.[2-3]

A promising method for delivering and enhancing the bioavailability of hydrophobic medications and bioactive food ingredients found in blood plasma is the use of nanoemulsion drug delivery devices. Most medications have a hydrophobic (lipophilic) character, which causes issues with bioavailability and limited solubility.[4-5]

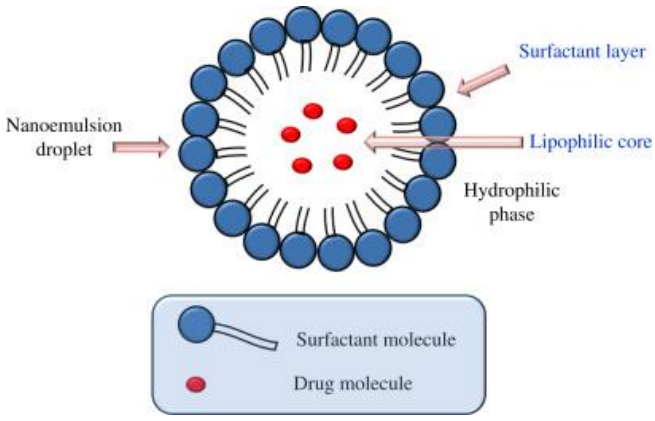

Figure: 1 Structure of Nanoemulsion

TYPES OF NANOEMULSION

Nanoemulsions are nano size emulsions dispersed in a continuous phase. They are non-equilibrium systems that are kinetically stable but not thermodynamically stable. Two main types of nanoemulsions are oil-in-water (oil droplets in aqueous phase) and water-in-oil (water droplets in oil phase) nanoemulsions. They can be used to solubilize various hydrophobic and hydrophilic substances that originally have low solubility in the continuous phases. There are also more complex nanoemulsions such as water-in-oil-in-water multiple emulsions.[6]

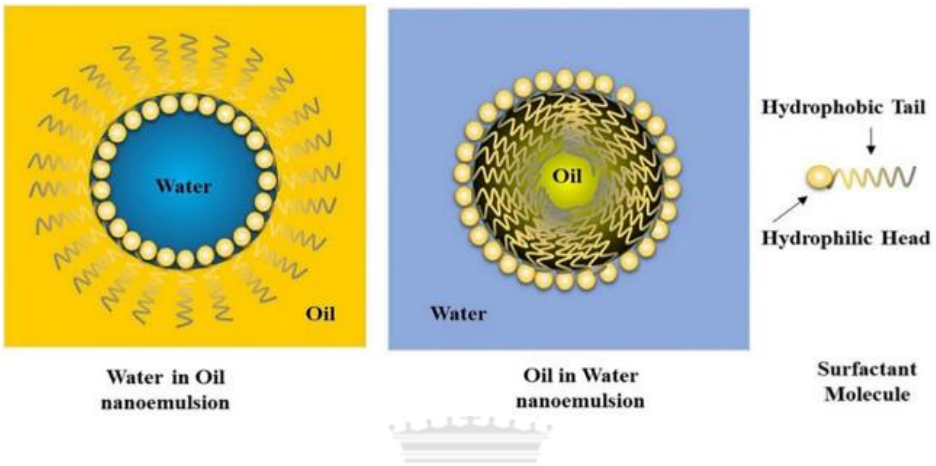

Figure: 2 Types of Nanoemulsion

BENEFITS OF NANOEMULSION

- Nanoemulsions are a useful transport method because of their increased surface area and free energy.
- The issues with natural creaming, flocculation, coalescence, and sedimentation are not evident.
- It can be made in many different forms, including foams, creams, liquids, and sprays.
- They are non-toxic and non-irritating, making it simple to apply the mucous membranes and skin.
- If the formulation includes biocompatible surfactants, it can be taken orally.

- It is suitable for both human and veterinary medicinal uses because it does not harm healthy human and animal cells. You can use it to replace vesicles and liposomes, and you can create lamellar liquid crystalline phases to enclose the nanoemulsion droplets.

- Nanoemulsions can penetrate the "rough" skin surface because of their small size, which improves the penetration of active ingredients.

- It is the first stage in the manufacture of nanospheres and nanocapsules employing interfacial polycondensation and nano precipitation It enables toxicity studies of oil-soluble medications and greater uptake of oil-soluble nutrients in cell cultures to increase proliferation of cultured cells.[7-9]

DRAWBACKS OF NANOEMULSION

- In order to stabilise the nanodroplets, a high concentration of surfactants and cosurfactants must be used.

- Limited ability to dissolve compounds with high melting points.

- For use in pharmaceutical applications, the surfactant must be Non-toxic.

- The stability of nanoemulsions is affected by environmental factors including pH and temperature. When patients receive nanoemulsion, these variables alter.[10]

COMPONENTS OF NANOEMULSION

Main three components of Nanoemulsions are as follows:

- Oil

- Surfactant/Co-surfactant

- Aqueous phase[11]

FORMULATION ASPECTS FOR NANOEMULSION

Since nanoemulsions have a very small particle size range, they can be most effectively produced using high-pressure equipment.[12]

1. High Pressure Homogenization

The preparation of nanoemulsion requires the use of a high pressure homogenizer. This technique produces nanoemulsions of low particle size i.e. 10-100nm. The dispersion of (oily and aqueous phase) is achieved by forcing their mixture through a small inlet orifice at a high pressure (500 to 5000 psi), which subjects the product to intense turbulence and hydraulic shear resulting in extremely fine particles of emulsions. The particles which are formed exhibit a liquid, lipophilic core separated from the surrounding aqueous phase by a monomolecular layer of phospholipids.[13]

2. Spontaneous Emulsification

It involves three main steps: 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 giving o/w emulsion. The water-miscible solvent was removed by evaporation under reduced pressure.[14]

3. Solvent Evaporation Technique

This technique involves preparing a solution of drug followed by its emulsification in another liquid that is non-solvent for the drug. Evaporation of the solvent leads to precipitation of the drug. Crystal growth and particle aggregation can be controlled by creating high- shear forces using high-speed stirrer.[15]

4. Hydrogel Method

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.[16]

5. Microfluidization

Microfluidization is a patented mixing technology, which makes use of a device called microfluidizer. This device uses a high-pressure positive displacement pump (500 - 20,000 psi), which forces the product through the interaction chamber, consisting of small channels called "microchannels". The product flows through the micro- channels on to an impingement area resulting in very fine particles of submicron range. The two solutions (aqueous phase and oily phase) are combined together and processed in an inline homogenizer to yield a coarse emulsion. The coarse emulsion is introduced into a microfluidizer where it is further processed to obtain a stable nanoemulsion. The coarse emulsion is passed through the interaction chamber of the microfluidizer repeatedly until the desired particle size is obtained. The bulk emulsion is then filtered through a filter under nitrogen to remove large droplets resulting in a uniform nanoemulsion. High- pressure homogenization and microfluidization can be used for fabrication of nanoemulsions at laboratory and industrial scale, whereas ultrasonic emulsification is mainly used at laboratory scale.[17]

6. Ultrasonication

In this technique premixed emulsion is exposed to agitation at an ultrasonic frequency of 20 kHz reducing the droplets to nanodroplets size. The resultant emulsion is then passed through high shear region to form droplets with uniform size distribution. Water jacket is employed in this technique to regulate the temperature. Sonotrodes also known as sonicator probes consisted of piezoelectric quartz crystals as the energy providers during ultrasonic emulsification. On application of alternating electric voltage, these sonotrodes contract and expand. Mechanical vibrations are produced when the sonicator tip contacted the liquid resulting in cavitation, which leads to collapse of vapour cavities formed within the liquid. This technique is mainly adopted when droplet size less than 0.2 μ is required. Shi et al. formulated emodin-loaded nanoemulsion by using an ultrasonic emulsification method at a frequency of 25 kHz and achieved mean diameter of emodin loaded nanoemulsion was found to be in the range of 10- 30 nm.[18]

7. Phase inversion method

In this method, fine dispersion is obtained by the use of chemical energy resulting from phase transitions produced by the emulsification pathway. The phase transition is produced by varying the composition of the emulsion and keeping temperature constant or vice versa.[19]

FACTORS AFFECTING THE FORMULATION OF NANOEMULSION

❖ The Nanoemulsion's most crucial component is the surfactant. They shouldn't create lyotropic liquid crystalline "microemulsions" phases. Phases that are typically utilised with the co-surfactant are systems with short chain alkanes, alcohols, water, and surfactants.

❖ To prevent Oswald ripening, the composition must be appropriate, and the dispersed phase must be almost completely insoluble in the dispersion medium.

❖ Surfactants that are present in excess make it possible to coat new nanoscale surfaces quickly during emulsification, which prevents induced coalescence.[20]

TECHNIQUES FOR CHARACTERIZATION NANOEMULSION [21-24]

Numerous physicochemical criteria, including morphology, refractive index, particle size and distribution, zeta potential, percentage transmittance, dilution test, emulsifying time, dye test, drug content, and viscosity, were used to characterise nanoemulsions.

Morphological characteristics

Transmission electron microscopy was used to analyse the surface morphology of the artemether-loaded nanoemulsion.

Particle size

The optimised formulation's globule size and size distribution (PDI) were measured using the Delsa Nano C Zeta Sizer and photon correlation spectroscopy. 2 ml of nanoemulsion was put into Beckman Coulter cuvettes for the purpose of measuring globule size and PDI, and measurements were taken.

Particle charge (zeta potential)

Particle charge determines the physical stability of the nanoemulsion. Particle charge is quantified as zeta potential value which is measured via electrophoretic mobility of particles in an electrical field. Zeta potential of optimised formulation was measured using Beckman coulter Delsa™ Nano C particle analyzer.

Percentage transmittance

The Shimadzu UV/VIS spectrophotometer was used to calculate the percentage transmittance. Double distilled water was used to dilute one millilitre of the formulation 100 times before it was examined at 210 nm against water as a blank.

Refractive index

Using a refractometer of the Abb type, the refractive index of a few selected formulations was calculated.

Dilution test

To check for the nanoemulsion's phase inversion, a dilution test was conducted. Phase inversion was looked for by diluting 1 ml of the optimised nanoemulsion with 10 ml of water in a test tube.

Dye solubility test (o/w test)

A few drops of the water soluble dye (Eosin yellow) were added and thoroughly mixed with 1 ml of nanoemulsion in an eppendorf. Under a fluorescent inverted microscope, the formulation was examined.

Emulsifying time

Emulsification time was calculated using a slightly modified version of the approach provided by. This was accomplished by mixing 200 ml of milli-Q water and 0.3 ml of self-emulsifying oil formulations at 37 °C in a beaker. The sample was swirled while being visually observed to gauge when the emulsion had fully formed.

Drug content

By dissolving 1 ml of the formulation in 10 ml of methanol, the drug content of the nanoemulsion formulation was determined. After that, this mixture spent 30 minutes in a shaking incubator (50 rpm, 37 0.5°C). After 30 minutes, the supernatant was gathered and subjected to an analysis using a UV spectrophotometer (against methanol as a blank).

Viscosity

In order to measure the viscosity of the nanoemulsion, 1 ml of the formulation was sheared at a rate of 100 s1 for 10 minutes at a temperature of 37 0.5°C while the spindle speed was set to 100 rpm.

STABILITY STUDIES [25-26]

The stability study is an important criteria to take into account when judging nanoemulsions. Nanoemulsions are distinguished from other dispersed systems by their higher stability.

Thermodynamic stability studies

Thermodynamic stability studies: In these types of stability studies, the chosen samples are put through a variety of tests to determine how stable they are physically. The procedure involves three cycles: first, heating and cooling cycles are repeated six times; next, heating and cooling cycles alternate at 40°C and 4°C; last, centrifugation at 3500 rpm for 30 min. Phase separation-related changes in the formulation are monitored throughout each cycle.

Accelerated stability studies

Studies of accelerated stability are carried out on the improved formulation. Studies on stability under increased temperature and humidity are referred to as accelerated stability studies. Glass vials containing three batches of the nanoemulsions were maintained at ambient humidity levels 23 at three different temperatures of 30°C, 40°C, and 60°C. The samples are subsequently evaluated in relation to ICH stability standards.

APPLICATIONS OF NANOEMULSION [27]

a. Nanoemulsions in drug delivery

The majority of drug delivery methods, including topical, ophthalmic, intravenous, internasal, and oral delivery, involve nanoemulsions. These uses make use of nanoemulsions' lipophilic properties to dissolve medications that aren't soluble in water as well as their customizable charge and rheology to create aqueous solutions that may be administered to patients with ease.

b. Nanoemulsions in food industry

In the food industry, nanoemulsions can be used to create foods containing components that are otherwise challenging to incorporate because of poor water solubility. One such ingredient is -carotene, a pigment that gives plants like carrots their colour and has significant health advantages.

c. Nanoemulsions as building blocks

Nanoemulsions can be utilised as building blocks for the creation of more sophisticated materials by taking advantage of their small size and large surface area, which make it simple to decorate a liquid-liquid surface with functional moieties like designer macromolecules.

d. In Cosmetic

The aesthetic qualities of nanoemulsions, such as their low viscosity and transparent visual characteristics with droplet sizes below 200 nm, as well as their large surface area that enables efficient transport of the active component to the skin, make them particularly alluring for use in cosmetics. Because there is no intrinsic creaming, sedimentation, flocculation, or coalescence, which is seen with macro emulsions, nanoemulsions are suitable in cosmetics. Using high-energy machinery can prevent the introduction of potentially irritating surfactants during manufacture. It might be helpful for moisturising, anti-aging, and suncare products. Giving skin care products a pleasant skin feel is helpful.

CONCLUSION

The distribution of pharmaceuticals, biologicals, or diagnostic agents is made easier by the use of nanoemulsion formulations. For more than 40 years, clinics have been using Nanoemulsions as fluids for whole parenteral feeding. Several additional medication delivery products. Recent developments in the creation of nanoemulsions hold considerable promise for both nanomedicine and nanocosmetics. Nanoemulsion has proven to be a highly effective method of delivering APIs to a variety of biological targets, including mucosal or epithelial surfaces. For delivering and concentrating herbal bioactives and extracts, nanoemulsions have been employed. Drugs and food ingredients that are hydrophobic and have a high First - Pass metabolism have a low bioavailability downside that is successfully addressed by nanoemulsion drug delivery devices. In terms of pharmacological, biological, or diagnostic agent administration, nanoemulsion formulations exhibit a number of benefits. Additionally, they safeguard labile drugs, improve drug solubility, improve bioavailability, enable regulated medication release, and lower patient variability.

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Author -1	**Nivetha.M,** Assistant Professor, Department of Pharmaceutics, Excel College of Pharmacy, Komarapalayam, Namakkal -637303, Tamilnadu, India.
Author -2	**Karthick.M,** Assistant Professor, Department of Pharmaceutics, Excel College of Pharmacy, Komarapalayam, Namakkal -637303, Tamilnadu, India.
Author -3	**Divyaparvathi.R,** Assistant Professor, Department of Pharmaceutics, Excel College of Pharmacy, Komarapalayam, Namakkal -637303, Tamilnadu, India.
Author -4	**Manivannan.R,** Professor & Principal, Department of Pharmaceutics, Excel College of Pharmacy, Komarapalayam, Namakkal -637303, Tamilnadu, India.
Author -5	**Bagathsingh.C, Deivasundari.P, Nagarajan.V, Srinivas.P, Surendharan.P** B.Pharm Final Year Student, Excel College of Pharmacy, Komarapalayam, Namakkal -637303, Tamilnadu, India.