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"A REVIEW ON NANOEMULSION : AN ADVANCED DRUG DELIVERY SYSTEM"

[1]Mr. Amol D. Igave, [2]Mr. Manoj Jayebhaye, [3]Ms.Shraddha Pathak, [4] Ms. Dipali Khandagale

[1]B.pharmacy (final year) RMP's Bhalchandra College Of Pharmacy, Pune, [2]Assistant professor of RMP's Bhalchandra College Of Pharmacy, Pune , [3]Assistant Professor of RMP's Bhalchandra College Of Pharmacy, pune , [4] Assistant Professor of RMP's Bhalchandra College of.Pharmacy

B.Pharmacy(final year),[1]Bhalchandra College Of Pharmacy, Pune, India

Abstract :

Nanoemulsions preparation is advanced drug delivery systems. Nowadays many lipophilic drugs are present in nature for the delivery of this drug, Nanoemulsions are prepared.Nanoemulsions are colloidal dispersion systems are thermodynamically stable systems in which two immiscible liquids i.e. oil and water are mixed together to form a stable liquid. Stability occurs due to the addition of proper emulsifying agents i.e. Surfactant and Co-surfactant. Nanoemulsions are emulsions made of nanosized particles having size ranges from 5 nm to 200 nm that are intended to enhance the delivery of active drugs. These are clear, transparent systems. These are used in the pharmaceutical industries because it increases the solubility and bioavailability of lipophilic drugs. But hydrophilic drugs have poor bioavailability in oral route . Mainly solid forms of Self Nanoemulsifying Drug Delivery Systems are used to improve the solubility and bioavailability of poorly water soluble drugs. SNEDDS are isotropic,transperant mixture of oil,surfactant (HLB>12) and cosurfactant. Nanoemulsions have good kinetic stability. This review gives the detail information about preparation, mechanism, biopharmaceutical aspects, applications of nanoemulsions for enhancement of bioavailability of poorly water soluble drugs.

Keywords:. Nanoemulsion, pseudoternary phase , ultrafine emulsions

INTRODUCTION

Nanoemulsions are novel drug delivery systems are characterised by uniform small droplet sizes, usually between 5-200nm and gives controlled and sustained release. Their small droplet size gives them a transparent and translucent appearance. Nanoemulsions are thermodynamically unstable systems which can be stabilized by the addition of proper emulsifying agent (emulsifier). They consists of two phases i.e. dispersed phase or discontinuous phase and dispersion medium or continuous phase.

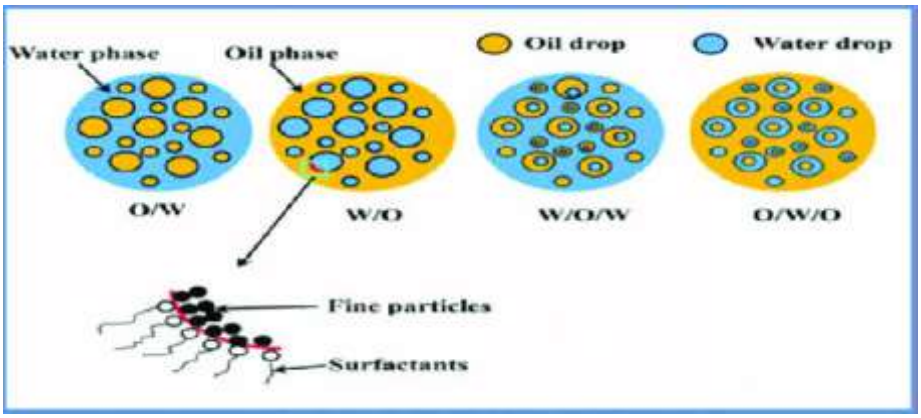
On the basis of phases, Nanoemulsions are classified into three types

Types of Nanoemulsion:

1.W/O (water-in-oil) nanoemulsions : Nanoemulsions in which the water is discontinuous phase and oil is continuous phase. Water droplets are dispersed in the continuous oily phase.

2.O/W (oil-in-water) Nanoemulsions : Nanoemulsions in which the oil is discontinuous phase and water is continuous phase. Oil droplets are dispersed in the continuous water phase.

3.O/W/O or W/O/W or Multiple Nanoemulsions : In this Nanoemulsions , both oil and water droplets are interspersed through the system.



➢ **Components of Nanoemulsion**

• Oil

• Surfactant and Co-surfactant

• Aqueous phase

Nanoemulsions are colloidal dispersion systems which consists of oil phase , aqueous phase, surfactant and cosurfactants in proper ratio. The selection of oil is very important factor during the formulation of nanoemulsion. All the components should be compatible to each other. The oil which is selected should able to dissolve the substances used in the dosage form to get higher solubility and bioavailability.The surfactant are used to decrease interfacial tension which occurs between the solid and liquid.

➢ **Advantages of nanoemulsion :**

•.It improves the solubility of water insoluble drugs.

•.Drug absorption variability can be reduced.

•.Less amount of energy is required for the preparation.

•.It increases the permeability of drug into skin.

• It is nontoxic and non irritant in nature.

• It is used to mask the unpleasant taste.

• It can be formulated in a variety of formulations like gels , ointments, liquids, sprays and creams.

➢ **Disadvantages of nanoemulsion :**

• The preparations of Nanoemulsions are required the high pressure homogenizers and ultrasonic equipments.

• It requires the surfactant and cosurfactant in large amounts for the stability of Nanoemulsions.

• Stability of nanoemulsion is affected by environmental factors like pH and temperature.

METHODS OF PREPARATION OF NANOEMULSION :

The various methods for the preparation of nanoemulsion include two methods : (a) high energy emulsification and (b) low energy emulsification. The high energy emulsification method includes high pressure homogenisation, ultrasonic emulsification, microfluidization and membrane emulsification. The low energy emulsification method includes phase inversion temperature and spontaneous emulsification.

A.High pressure homogenization :

This method involves the use of high pressure homogenizer/piston to produce nanoemulsion of extremely low particle size (up to 1 nm). In a high pressure homogenizer , the dispersion of both phases i.e.oil and water is achieved by forcing their mixture through a small inlet proficiency at very high pressure 500 to 5000 psi

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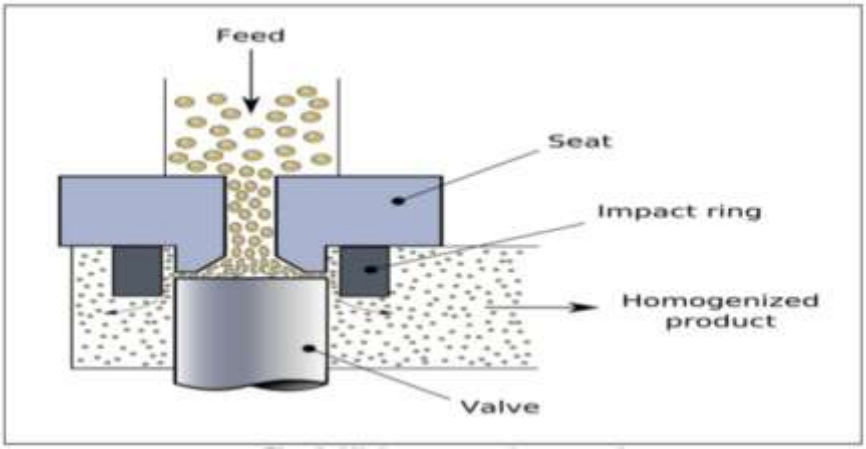
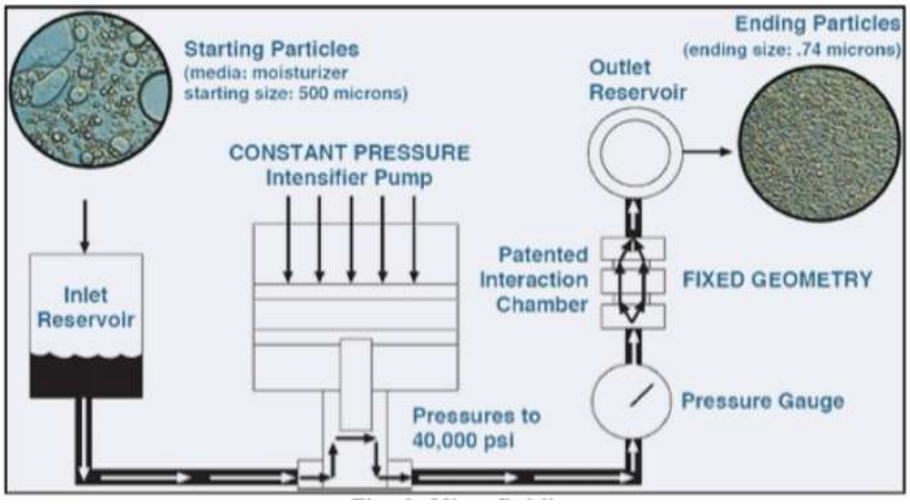
B.Ultrasonic emulsification :



Ultrasonic emulsification is effectively used in reducing the droplet size. In this method, the energy is provided through sonotrodes called as sonicator probe. It contains piezoelectric quartz crystal which can contract and expand in response to alternating electric voltage. Sonicator produces mechanical vibration and removes cavities present between liquid. Thus, the ultrasound can be directly used in the preparation of nanoemulsion.

C. Microfluidization

In this method, the instrument which is used known as microfluidizer. This instrument uses high pressure which forces the drug product through the interaction chamber resulting in very fine particle of submicron range. This process is repeated for several times to obtain desired particle size to produce nanoemulsion.



D. Phase inversion temperature

This method involves the change in phase by applying a higher temperature to a microemulsion. In this method, the adequate phase transitions is obtained by changing the composition of oil and aqueous phase at constant temperature or also by changing the temperature at composition.

E. Spontaneous emulsification

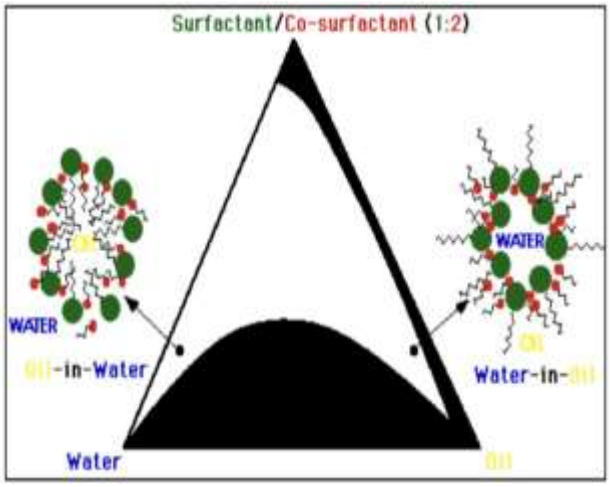
It involves three steps : a) preparation of homogeneous organic solution consisting of oil and lipophilic surfactant in water miscible solvent and hydrophilic surfactant, b) the organic phase is injected in aqueous phase under continuous magnetic stirring, o/w emulsion is formed, and (c) the aqueous phase is removed by evaporation under reduced pressure.

Characterization of nanoemulsion:-

A.Particle size analysis: The particle size is measured by particle size analyzer. It is important to measure the particle size. Nanoemulsions are analyzed for particle size and size distribution by the light scattering method.

B. pH measurement : Digital pH meter is used to determine the pH of the nanoemulsions

C. Phase behaviour study : Phase behaviour study is necessary for those Nanoemulsions that are prepared by phase inversion temperature and self emulsification method and used to determine the phase of nanoemulsion, dispersibility and for the optimisation of ingredients (surfactant, oil phase and aqueous phase) . This study is done by placing the different ingredients of nanoemulsion in glass ampoules at varying the concentration. Then all ingredients are thoroughly homogenised at a certain temperature for a time until equilibrium. An isotropic phase can be identified by polarized light is used to identify an isotropic phase.



D. Refractive index: This study is done by using an abbés refractometer.

RECENT ADVANCES AND INNOVATIONS :

Nanoemulsions have become a cutting-edge drug delivery system with several benefits, especially when it comes to improving the bioavailability and targeting of medications. In order to address issues with stability, toxicity, and targeting, there have been notable developments and breakthroughs in the creation, processing, and use of nanoemulsions throughout the last ten years. Here are a few of the most significant recent developments:

1.**Novel Surfactant Systems**

Although surfactants have historically been essential for stabilizing nanoemulsions, the introduction of synthetic surfactants has sparked worries about toxicity, especially when administered parenterally. The goal of recent advancements is to identify safer, more biocompatible substitutes.

2.**Stimuli-Responsive Nano emulsions**

Stimuli-responsive Nano emulsions are a major area of innovation, where the release of the drug is triggered by specific physiological or environmental factors. This approach allows for more precise control over the timing and location of drug release. Some recent advances in this area include:

a)PH-Responsive Nano emulsions: pH-sensitive Nanoemulsions can be designed to release their drug payload in specific regions of the body with varying pH levels (e.g., the acidic environment of the stomach or the more alkaline environment of the small intestine). Chitosan-based Nano emulsions and polymers like poly (acrylic acid) are widely used to achieve pH-sensitive release mechanisms.

b)Temperature-Responsive Nano emulsions: These Nano emulsions release their therapeutic payload in response to temperature changes. This can be particularly useful for thermally unstable drugs, or in hyperthermia-based cancer treatments where local temperature is raised to enhance drug delivery. For example, the use of poly (N-isopropyl acrylamide) (PNIPAAm) has shown promise in temperature-sensitive drug release.

c)Magnetic-Field-Responsive Nano emulsions: Incorporating magnetic nanoparticles into Nano emulsions enables magnetically guided drug delivery. In this approach, a magnetic field is applied to direct the drug-loaded Nano emulsions to specific sites in the body (e.g., tumors or inflamed tissues), allowing for localized and targeted drug release. This is particularly valuable in oncology and site-specific therapy.

d)facilitating gene therapy or the delivery of biologic drug.

3. Nanostructured Lipid Carriers and Hybrid Systems

Innovative approaches are combining Nano emulsions with other lipid-based nanocarriers to improve drug solubility, stability, and bioavailability. These include:

a)**Nanostructured Lipid Carriers (NLCs)**: NLCs are an improvement over traditional lipid emulsions and offer a more stable structure, which helps encapsulate drugs that are poorly soluble in water. Recent work on combining Nano emulsions with NLCs has resulted in formulations that can encapsulate both hydrophobic and hydrophilic drugs. These hybrid systems are particularly useful in **controlled release** and **long-term drug delivery**.

β)**Lipid-Core Micelles**: Lipid-core micelles, which consist of a lipid core surrounded by a shell of surfactants, are being used for delivering hydrophobic drugs with high loading capacities. These Nano emulsion-micelle hybrid systems can also offer prolonged circulation times and better protection for sensitive drugs (e.g., proteins, peptides).

4. **Gene and Protein Delivery**

One of the most promising areas of development for Nano emulsions is their application in **gene delivery** and the delivery of **bio therapeutics** (e.g., monoclonal antibodies, vaccines). Recent innovations include:

α)**Gene Therapy**: Nano emulsions are being engineered to deliver nucleic acids (DNA, RNA, siRNA) to target cells. This is particularly important for the delivery of **gene editing tools** such as **CRISPR-Cas9**, which require precise and efficient delivery systems. Recent formulations are designed to overcome the challenges of protecting the genetic material from degradation and facilitating cellular uptake.

CONCLUSION :

Nanoemulsion is a novel drug delivery system designed for improving solubility, absorption and bioavailability of poorly water soluble drugs. It enhances the dissolution of the drugs due to increased surface area. Nanoemulsion may also protect the drugs from hydrolysis and oxidation. There are various advantages of formulation of nanoemulsion like delivery of drugs, biological and diagnostic agents. Overall all nanoemulsion formulation may be considered as effective, safe and with increased bioavailability.

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