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A Review on Nanoemulsion: A Novel Drug Delivery Systum

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ABSTRACT:
Nanoemulsions are submicron-sized emulsions that are being investigated as drug carriers to improve the delivery of therapeutic agents. These are thermodynamically stable isotropic systems in which two immiscible liquids form a phase by mixing with appropriate surfactants and co-surfactants. Nanoemulsion droplet sizes are generally in the range of 20-200nm, showing a narrow droplet size. This article focuses on providing a brief introduction to the design, preparation, process, measurement, and various nanoemulsions used in the preparation of nanoemulsions such as microfluidization, high-pressure homogenization, low-energy emulsification, evaporation techniques and are used for properties such as particle size analysis, viscometry, chemical content, pH measurement, zeta potential, transmission electron microscopy, thermal stability, release and in vitro skin penetration. These are made for medical purposes.

I. INTRODUCTION[1-5]

Nanoemulsion is an emulsion with a droplet size of 20-200nm. A traditional NEs consists of oil, water and emulsifiers. The addition of an emulsifier is important for creating small droplets because it reduces the interfacial tension between the oil and water phases of the emulsion, or the surface energy of an area. Emulsifiers also stabilize NEs through repulsive electrostatic interactions and steric hindrance[1]. Also available. High energy and low energy High pressure homogenizationHigh energy methods such as (HPH) and ultrasound use a lot of energy water is small On the other hand, low energy Special equipment is used for consumption. Create small droplets that do not use much energy. Phase inversion temperature (PIT) and emulsion inversion point (EIP) are two examples of low energy consumption for the formation of NEs. The oil/water interface and evaporative ripening have also been developed to create NEs.[2-3]

Nanoemulsions are stable against emulsification due to their small size, and Ostwald ripening is important information for the decomposition of NEs. The main application of nanoemulsions is the preparation of nanoparticles using polymerizable monomers as dispersed phase (so-called miniemulsion polymerization method), in which NEs droplets act as nanoreactors.[4]

Another interesting application being developed is the use of nanoemulsions as templates, for example for controlled drug delivery and targeting. The main application of nanoemulsions is the preparation of nanoparticles using polymerizable monomers as a dispersed phase, where NEs droplets act as nanoreactors.[5]

1.1 TYPES[6-7]:

According to the relative composition and distribution of the ubiquitous continuous phase and dispersed phase, nanoemulsions are divided into two-phase (O/W or W/O) or multiphase nanoemulsions. Nanoemulsion droplet count and overall strength are determined by the phase volume fraction, which also reflects the relative correlation between the internal and external phases that make up the NEs[6]. To determine which type of NEs fits the parameters, the interactions between the various components that make up the NEs need to be predicted. O/W emulsification is good when the emulsifier is hydrophilic and vice versa; for example, if the emulsifier is lipophilic. In general, the polar region of an emulsifier provides a better barrier to coupling than the hydrocarbon region.[7]

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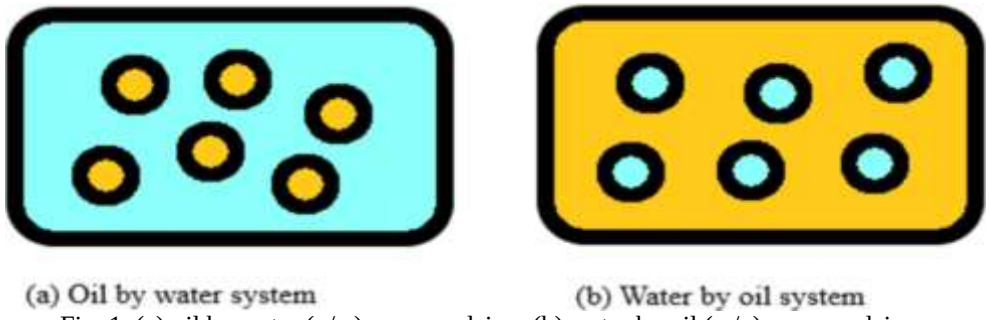

Fig. 1. (a) oil by water (o/w) nanoemulsion, (b) water by oil (w/o) nanoemulsion.

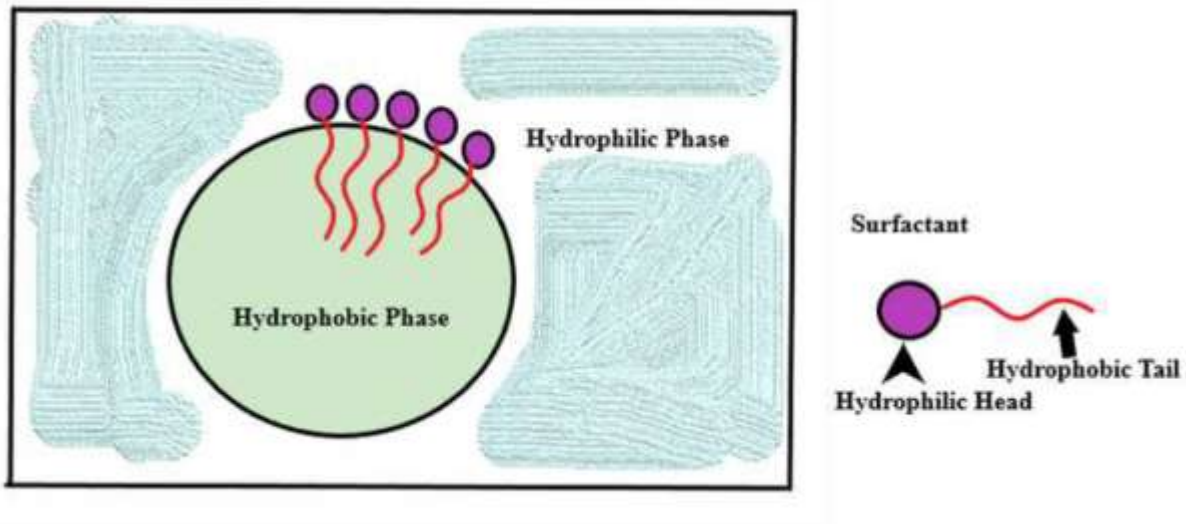

Fig. 2. Droplet stabilized by surfactant.

1.2METHOD OF PREPARATION[8-20]:

Nanoemulsions are produced using a variety of techniques, such as high-pressure homogenization, microfluidization, phase inversion, spontaneous emulsification, solvent evaporation, and hydrogel formation. Various emulsions are generally prepared using double emulsion-liquid evaporation systems. Various techniques have been used to characterize nanoemulsions used in drug delivery. Only two main methods are used in the formation of nanoemulsions: (a) persuation method and (b) brute force method.

(a)Persuasion method/phase inversion technique[9-11]**:**The NEs interaction between the device does not require an external force, but changes according to the growth phase caused by temperature change or the growth of cracks such as the structure during the process, so that the boundaries of the others remain intact.Methods of persuasion can be broadly classified as,

A. Phase transition from near-optimum state via change in single variable, Change of one formulation variable, such as temperature or salinity close to optimal value, is required for the phase transition from the near-optimum state. The ideal hydrophilic-lipophilic deviation (HLD) value for a system, such as a NEs made at a higher temperature, is close to the center.
B. Phase transition from the near-optimal state through the alteration of multiple variables, or formulation variables. For instance, using a higher temperature and adding more salt to NEs
C. Catastrophic inversion, a reversal of low inner stage emulsion with the goal that the inside stage converts to outer stage.
D. Phase transition stabilized by liquid crystal formation, Nanodroplets are stabilized from a state close to HLD-0 by the formation of liquid crystals, which stabilizes the phase transition.

(b)Brute force method[15-16]**:**This method uses energy to break down oil droplets down to the nanoscale. High-pressure homogenizers, high-speed mixers, small-pore membranes, and high-frequency ultrasonic devices are some of the tools

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used to create nanoemulsions. The operating variables (emulsification time, mixing degree, input power, and emulsification method) and the combination of variables affect nanoemulsion properties such as size, visibility, and high kinetic stability. Using high-pressure equipment, high-pressure homogenization and microfluidization techniques are used to produce small-sized nanoemulsions in both commercial and experimental settings. Ultrasound and in situ emulsification are two methods to prepare nanoemulsions.

1.High pressure homogenization[13]:

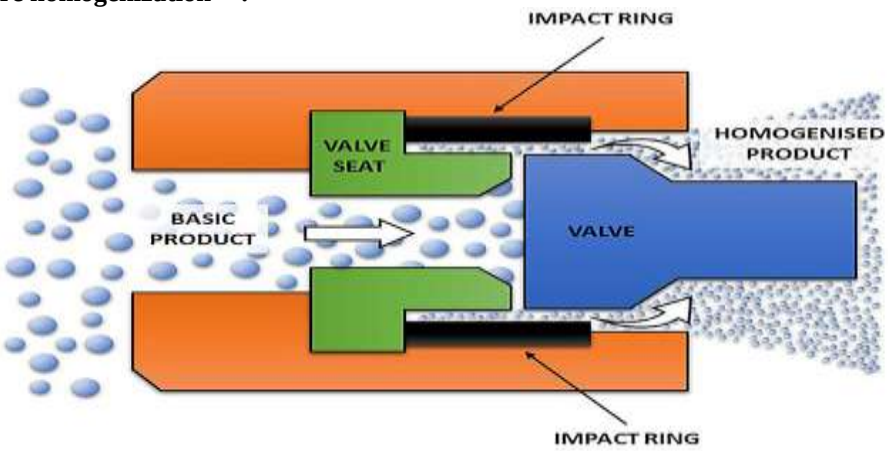

Figure Error! No text of specified style in document.**.1: High Pressure Harmonization**

A. Nanoemulsion preparation requires a high shear force, so a high-force homogenizer or piston homogenizer should be used in this method to produce small size (up to 1 nm) nanoemulsions. In this way, the mixture is forced through the orifice under low pressure ranging from 500 to 5000 psi. By applying additional turbulence and hydraulic shear to the finished product, an emulsion with excellent properties is created[12].

B. This has proven to be the most effective method of making nanoemulsions, but its only drawback is that it uses a lot of energy and causes the emulsion to heat up during operation. More homogenization is required to obtain smaller particle size[14]. proposed the preparation of Phyto sphingosine O/W nanoemulsions using high homogenization technique and found that the droplet size decreased after 8 homogenization cycles and this nanoemulsion remained stable for more than half a year[13].

2.Micro-fluidization[18-19]:

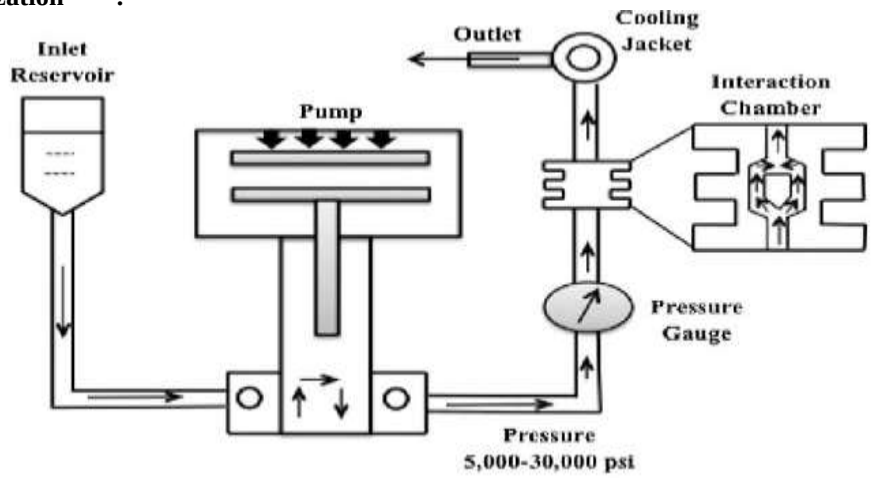

Figure Error! No text of specified style in document.**.2: Micro-fluidization**

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A. In this method, a device called a microfluidizer is used. It uses a high-pressure pump (500-20 000 psi) to push particles out of the chamber through stainless steel microchannels through the impact zone, producing particles in the submicron range[18].

B. The mixture is circulated several times in the microfluidic bed until it reaches the desired molecular size. The resulting product is further passed through a line to separate small beads from larger beads and obtain a nanoemulsion-like substance[18]. When a microfluidized bed was used to produce octadecane oil-in-water nanoemulsions, droplet size was found to decrease as the homogenization pressure and number of sections increased. Fractured nanoemulsion prepared by two-step homogenization. First, a coarse emulsion is prepared using a mixer and then processed using a microfluidizedbed[19].

3.Ultrasonication[16]: In this way, a premixed emulsion is agitated using an ultrasonic frequency of 20 kHz, thereby reducing the droplets to the size of nanodroplets. The resulting emulsion is then passed through the high shear zone to form uniform droplets. In this method, a water jacket is used to control the temperature. During the phacoemulsification process, a piezoelectric quartz crystal (also known as an ultrasonic generator or ultrasonic probe) serves as the energy source. The sonic electrodes expand and contract when AC voltage is applied. When the sonicator tips come into contact with the liquid, any vibration causes cavitation, causing the liquid vapor chamber to evaporate. This method is generally used when a hole size of less than 0.2 is required.

4.Spontaneous emulsification[20]: Using this method, nanoemulsions were prepared in three steps. The first step is to create a natural process containing oil and lipophilic surfactants in water-miscible soluble and hydrophilic surfactants, and then inject it into the water level below the beauty lotion combination to create O/W. Then, in the third stage, the organic solvent is removed using evaporation.

5.Solvent evaporation technique/hydrogel method[20]: In this way, the preparation and emulsification of other liquids that are not heavy on the drug and the evaporation of the solvent lead to the precipitation of the drug. Crystal growth and particle aggregation can be controlled using high-speed systems. The solvent evaporation method is similar to the hydrogel method. In this case, the miscibility of the solution with the antisolvent is the only difference in the solvent evaporation method.

1.3 ADVANTAGES[21] :

1. Reduces variation in absorption.
2. Increases the absorption rate.
3. Helps in solublizing lipophilic medication.
4. Dispenses drugs that are insoluble in water in an aqueous form.
5. makes it more bioavailable.
6. The product can be delivered via topical, oral, and intravenous methods.
7. Rapid and efficient penetration of the drug molecule.
8. Helps in taste covering.
9. Protects against oxidation and hydrolysis as a drug in the oil phase of and o/w emulsion.
10. Reduced energy consumption.
11. Patient compliance is improved with the liquid dosage form.
12. Nanoemulsions are thermodynamically stable systems that can self-emulsify beacuse their properties are unaffected by the procedure used.
13. Compounds that are hydrophilic and lipophilic are carried in nanoemulsions.
14. The use of nanoemulsions as delivery systems increases a drug's efficacy, enables a lower total dose, and minimizes side effects.

1.4 DISADVANTAGES[21] :

1. Utilization of a significant amount of surfactant and cosurfactant, which is required for the Nanodroplets' stabilization.
2. Restricted solubilizing limit with regards to high softening substances.
3. For pharmaceutical applications, the surfactant must not be toxic.
4. The pH and temperature of the surrounding environment have an impact on the stability of nanoemulsions. When patients receive Nanoemulsion, these parameters changes.

1.5 Characterization[21-30]:

Multicomponent lipid formulations need to be evaluated and characterized by in vitro, ex vivo and in vivo measurements. Various methods were used to determine and evaluate the feasibility of the nanoemulsion formulation process. It is difficult to characterize the entire formulation due to the limitations of each machine, but complete formulation information is necessary for successful commercial development[21]. Conductivity, viscosity and dielectric constant provide important

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information at the macro level. The following characteristics often describe different recipes.

1.visual appearance :Calibrated glass cylinders or glass cylinders can be used to evaluate uniformity of appearance and balance color[22].

2.Color, Odor, and Taste: This is particularly important for oral formulations. Changes in the background, especially the active ingredients, are often caused by changes in spheroid size, crystal behavior, and subsequent changes in globule size distribution. The taste, odor and color of certain ingredients may change, indicating chemical incompatibility[22].

3.density : The specific gravity or density of nanoemulsion formulations are two important factors. A decrease in the density of milk usually indicates that it contains air. The rate of temperature can be determined using a manometer[23].

4.Ph : Once sedimentation equilibrium is reached, the pH of a formulation is tested using a pH meter at a specific temperature to reduce pH drift or the accumulation of suspended particles on the electrode surface. It is not recommended to add neutral electrolytes to the external stage of pH value construction as it will affect the physical stability of the suspension[25].

5.phase behaviour study : The aim of this study is optimization and mixing (oil and water phase emulsifier). There is a frequent need to investigate micro/NE formulations prepared by the PIT method and the self-nanoemulsification method to determine the phase and distribution of nanoemulsions[28].

6.emulsion droplet polarity: It is the most important factor determining the emulsification effect. The polarization of fat globules is affected by HLB, chain length, fatty acid unsaturation, molecular weight of the hydrophobic moiety, and emulsifier content. The attraction and forced production of chemical compounds for oil or water is represented by polarity[30].

7.Dispersibility Study. ,is study, which was conducted using a typical USPXXII dissolution apparatus, was done to assess the eGectiveness of self-emulsi1cation of nanoemulsionformulations. 500 ml of the dissolution medium is filled with 2.1 ml of each formulation, and the temperature is kept at 37±0.5°C. For gentle agitation, a stainless-steel paddle is circulated at 50 rpm. A basic dissolution paddle made of stainless steel revolves at 50 rpm to provide light agitation. Using the grading method presented below[26-27], the in vitroperformance is evaluated visually of the nanoemulsionformulations.

1.6 Future scope :

Since their creation, nanoemulsions have proven to be versatile and effective new drug delivery systems. Due to their ability to dissolve non-polar reactive drugs, nanoemulsions have been designed as drug delivery agents for various purposes in the pharmaceutical market. The future of nanoemulsions is very bright in various medical disciplinesor in the production of skin or hair cosmetics. Nanoemulsions have many applications, includingdrug delivery, where they work well in biological materials and enable a variety of drug delivery methods. Parenteral delivery has been used to meet nutritional needs, control drug release, deliver vaccines, and target drugs to specific sites. The use of these devices for oral administration of drugs has many advantages and uses; The size of the droplets affects how well they are absorbed in the gastrointestinal tract. Nanoemulsions have also been studied for their use in ocular delivery, where drugs are better preserved than their solutions. Other effective ways to deliver the nanoemulsionScienti1ca 19such as pulmonary and transdermal routes. Although not much is known about the use of nanoemulsions in other fields, these disciplines, which include engineering, agriculture, chemical and physical research, have great potential. The cost of making nanoemulsions will decrease as new equipment for high-pressure homogenization becomes available and manufacturers begin to compete with each other. Fundamental research on the performance of emulsifiers in nanoemulsion production will lead to better emulsification systems and better emulsifier use. The ability to modify nanoemulsions for targeted delivery holds great promise in fundamental fields such as oncology, treatment of malignancies, and drug delivery to the brain.

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