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A REVIEW ON NON AQUEOUS NANO EMULSION

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ABSTRACT

In general, emulsions are of the water-in-oil or oil-in-water type, but emulsions may contain a polar liquid as one of the phases. Non-aqueous nanoemulsions are useful in many situations where the presence of water is not desired and in the formulation of active ingredients that undergo hydrolysis or oxidation in the presence of water. Anhydrous nanoemulsion is the subject of a stable non-aqueous nanoemulsion (NANE) design using cosmetically approved ingredients as a vehicle for water-sensitive active ingredients. The non-aqueous nanoemulsion is the subject of increasing dermal penetration and permeation and studying drug solubility and dermal bioavailability. For better compliance, non-aqueous nano emulsions will be incorporated into cosmetics or personal care products. A non-aqueous system with glycerin and olive oil stabilized with glycerol monostearate with co-surfactant was obtained. It was observed that the emulsification behavior is completely unpredictable and the conventional theory of emulsification and HLB system cannot be applied here. By implementing a pseudoternary phase curve, an optimized non-aqueous nanoemulsion is obtained. The non-aqueous nanoemulsion region is determined and further characterized for pH, rheology, globule size analysis, zeta potential and stability.

KEYWORDS: Non-aqueous nano emulsion, HLB, Pseudo-ternary phase curve, Zeta Potential.

INTRODUCTION

Non-aqueous nanoemulsion (NANE) useful for drug delivery and basically overcomes the problem of slow and incomplete dissolution of poorly water-soluble drugs with water-unstable and/or unpalatable drugs. An emulsion is one of the most convenient and advantageous formulations in which one of the liquid phases is water; however, the emulsion may be formulated without an aqueous phase to form anhydrous, nonaqueous emulsions/microemulsions or oil-in-oil emulsions. Such systems can replace conventional emulsions where the presence of water must be avoided. . Such systems can reduce inherent limitations and facilitate the formation of solubilized phases from which absorption can occur. Unfortunately, the main difficulty in formulating NANEs stems from the lack of suitable surfactant action data in relevant non-aqueous media, or even the lack of a suitable surfactant designed for such a specialized system.

Non-aqueous nanoemulsions may have pharmaceutical or cosmetic value if they consist primarily of edible, non-toxic components and can be formulated to exhibit a wide range of physical properties. Some possible uses may be as topical application bases for dermatology, especially for labile drugs, as emollient bases for cosmetic preparations or as nutritional preparations.

Emulsion: An emulsion can be defined as a two-phase system consisting of two immiscible liquids, one of which (the dispersed phase) is finely and uniformly dispersed as globules throughout the second phase (the continuous phase). Since emulsions are a thermodynamically unstable system, a third agent, an emulsifier, is added to stabilize the system.

Types of Emulsion

1. Water-in-oil emulsion: A water-in-oil emulsion is a type of emulsion where the continuous phase is usually hydrophobic materials such as oil and the dispersed phase is water. More than 95% of the oil emulsion formed in an oil field is of the W/O type. W/O emulsions contain three substances such as; solvent, surfactant and water.

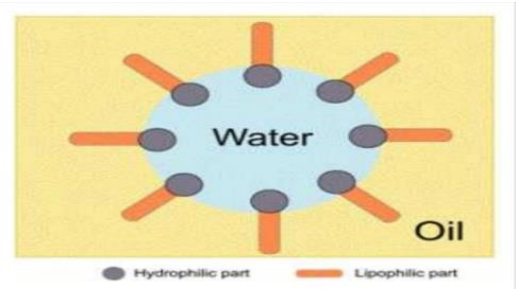

Fig.Water in Oil Emulsion.

2. Oil-in-water emulsion: In an oil-in-water emulsion, the oil droplets are dispersed in the aqueous phase. Fats or oils for oral administration are always formulated as oil-in-water (O/W) emulsions. Oil-in-water (O/W) emulsions are non-greasy and easily removed from the surface of the skin and are used externally for a cooling effect and internally to mask the bitter taste of the oil. Water-soluble drugs are released more quickly from an oil-in-water emulsion. O/W emulsions give a positive conductivity test like water, the outer phase being a good conductor of electricity.[9]

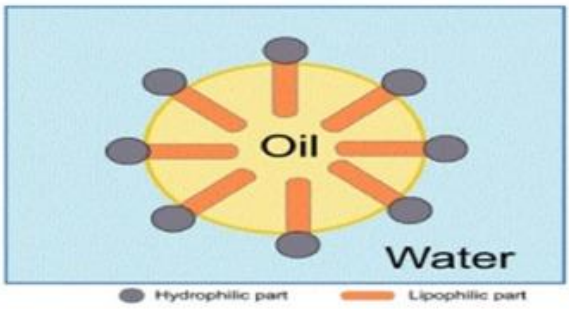

Fig.no.2. Oil in Water Emulsion.

3. Multiple emulsions: Multiple emulsions are more complex than their biphasic counterparts in terms of formulation, stability and drug release. They are a useful tool to achieve sustained drug release for various routes.

4. Pickering Emulsion: A type of emulsion stabilized only by solid particles located at the oil-water interface, was discovered a century ago, while it has been extensively studied in recent decades, replacing solid particles with traditional surfactants. Pickering emulsion is the most stable to coalescence and can acquire many useful properties.

Biological problems or disadvantages of non-aqueous systems

Very few biopharmaceutical studies have been conducted with Non-Aqueous Systems and there is a need for more comparative studies, especially against solid dosage forms. However, at this stage it is worth speculating on the issues that will affect absorption from non-aqueous systems. In the case of oral drug administration, the gastric emptying rate of nonaqueous systems is similar to that of solutions, making them particularly useful where rapid onset of action is desired. Conversely, if the therapeutic index of the drug is low, the rapid onset and accompanying high Tmax may lead to undesirable side effects

Method of preparation of non-aqueous nanoemulsion

Various methods are used for the preparation of nanoemulsions, including high-energy and low-energy emulsification methods, as well as combined methods. Of the high-energy methods, high-pressure homogenization, high-energy mixing, and ultrasonic emulsification are commonly used. Of the low-energy emulsification methods, attention is focused on the phase inversion temperature method, the point emulsion inversion method and the spontaneous emulsification method.

***1. Sonication Technique*: In the sonication technique, the size of the globules of a normal emulsion is made compact by using sonication mechanism. This method is utilized to develop a few quantities of batches of nano emulsion.**

***2. Solvent Displacement technique*:** In this technique, the non-aqueous phase is mixed with various water-miscible organic solvents like ethanol, acetone, etc. The aqueous and organic phases are mixed with the help of emulsifying agents to develop nano-emulsion by using rapid diffusion of organic solvent. Vacuum evaporation technique is then utilized to evaporate the organic solvent from the mixture.

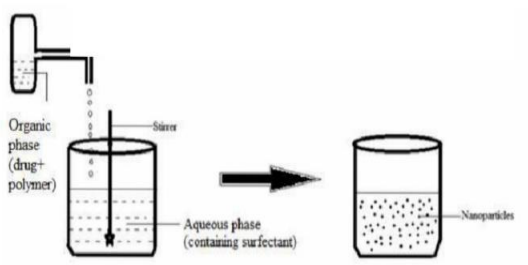

Fig. Solvent Displacement Technique.

3. High pressure homogenization method*:* This method is performed by applying a high pressure over the system having oil phase, aqueous phase and surfactant or co-surfactant. The pressure is applied with the help of homogenizer and the two liquids along with surfactant, co-surfactants are made to pass through a small orifice at high pressure (500- 5000 psi) to produce nano-emulsions. Some problems associated with homogenizer are poor productivity, component deterioration due to generation of much heat.

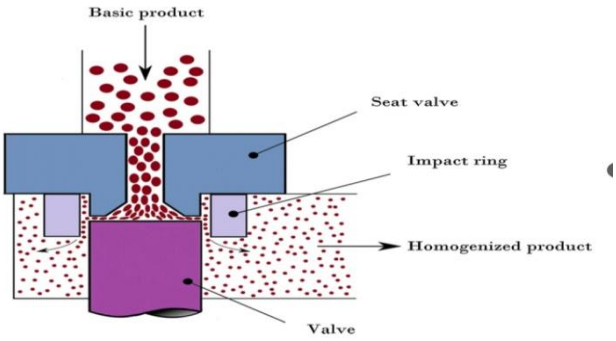

Fig.High Pressure Homogenizer.

***4. Phase Inversion Technique*:** This technique was based on the mechanism of changes of solubility of a surface-active agent such as polyoxyethylene with temperature. This surfaceactive agent is initially insoluble in lipids but changes into lipid-soluble by increasing temperature due to polymer chain dehydration. At a lower temperature, the surface-active agent monolayer has a better positive, spontaneous curvature producing oil swollen micellar solution phase.

Table No. 1: Oils used for formulating Non Aqueous Nano emulsions.

Castor oil	Coconut oil	Corn oil	Cottonseed oil
Primrose oil	Fish oil	Jojoba oil	Lard oil,
Linseed oil	Mineral oil	Olive oil,	Peanut oil
PEG-vegetable oil	Perfluro chemicals	Pine nut oil	Safflower oil
Sesame oil	Soybean oil	Sunflower oil	Wheat germ oil

Table No. 2: Emulsifiers for formulating Non Aqueous Nano emulsions.

Natural lecithin's	Phospholipids	PEG-phospholipids	Stearlyamine	Polyoxyethylene
Poloxamers (e.g. F68)	Polysorbates	Castor oil	Oley amine	Polyglycolized Glycerides

Table No. 3: Additives for formulating Non Aqueous Nano emulsions.

Antioxidant: a-tocopherol, Ascorbic acid
Tonicity Modifiers: Glycerol, Sorbitol, Xylitol
Buffering Agent: NaOH or HCl
Preservatives

Table No. 4: Type of Surfactants for formulating Non Aqueous Nano emulsions.

Ampholytic:
3-[N,N—Dimethyl (3-palmitoyl amino propyl) ammonia]-propane sulfonate
N-Dodecyl-N, N-dimethyl-3-ammonio-1-propane sulfonate
Sodium 2,3-dimercapto Propane sulfonate monohydrate
Zwitter ionnic:
3-(N, N-Dimethyloctylammonio) propane sulfonate
3-(N,N-Dimethyl palmitylammino) propane sulfonate
3-(Decyldimethylammonio) -propane- sulfonate
Anionic:
Cholic acid from ox or sheep bile.
Glycolithocholic acid ethyl ester
Lithium 3,5-diiodosalicylate
Cationic:
Girard's reagent 99%
N,N′,N′-Polyoxy ethylene(10)-N-tallow-1,3-diamino propane liquid
4-Nonyl phenoxy polyglycidyl ether
6-Cyclohexyl hexyl β-D-maltoside
Non-Ionic:
Glucopone 215,600 CS UP and 600,650 EC
Triton CF 10, N-57, 60, X-100, 207, 45,305,405.
Triton X-15
Tergitol NP-9
Tween (Polysorbate) 20,21,40, 60,61,65,80,81,85

Evaluation Parameters of Non-Aqueous Nano emulsions

1. Droplet Size Analysis: Droplet size analysis of nanoemulsion is measured by a diffusion method using a light-scattering, particle size analyser counter, LS 230. It is also measured by correlation spectroscopy that analyzes the fluctuation in scattering of light due to Brownian motion. Droplet size analysis of nanoemulsion can also be performed by transmission electron microscopy (TEM).

***2. Viscosity Determination*:** The viscosity of nanoemulsion is measured by using Brookfield-type rotary viscometer at different shear rates at different temperatures.

***3. Dilution Test*:** Dilution of a nanoemulsion either with oil or with water can reveal this type. The test is based on the fact that more of the continuous phase can be added into a

nanoemulsion without causing the problem of its stability. Thus, an o/w nanoemulsion can be diluted with water and a w/o nanoemulsioncan be diluted with oil.

***4. Zeta potential*:** An instrument named Zeta PALS is utilized to calculate Zeta Potential. Zeta Potential is the electrokinetic potential difference on the surface of the globule in nano-emulsion. Surfactant develops surface charges; however, additionally, act as a mechanical barrier.

***5. Drug Content*:** Pre-weighed nanoemulsion is extracted by dissolving in a suitable solvent, extract is analyzed by spectrophotometer or HPLC against standard solution of drug.

***6. Refractive Index*:** Refractive index of nanoemulsion is measured by Abbes refractometer.

7. PH: The pH of nanoemulsion can be measured by pH meter.

Advantages of Non-Aqueous Nano Emulsion

1. Non-aqueous nano-emulsion has high drug loading capacity.
2. Non-aqueous nano- emulsion increases the bioavailability of the drug.
3. Non-aqueous nano- emulsion can be used as carriers for lipophilic compounds.
4. Convenient for Parenteral, topical, ocular and oral administration.
5. Non-aqueous nano-emulsion as a potential for controlled drug release.
6. Non-aqueous nano-emulsion can be used for water unstable compounds.

Disadvantages of Non-Aqueous Nano Emulsion

1.Surfactants/co-surfactants concentration required for stabilization of nano-emulsions may be more extensive.

2. Change in pH and temperature may affect the stability of nano-emulsions.

3. Due to Oswald ripening effect, instability of nano-emulsion may be observed.

4.Cost of nano-emulsion is more because of the size reduction of disperse phase globules.

Application of Non-Aqueous Nano Emulsion

***1. Parenteral Delivery*:** This is the most common and effective route of drug administration for the drug with low bioavailability and narrow therapeutic index. Nano emulsions are more advantages for i v administration, due to the strict requirement of this route of administration, particularly the necessity for the formulation droplet size lower than 1 micrometre

2. Oral Drug Delivery System: Nano-emulsion is ideal in carrying of drugs such as hormones, steroids, antibiotics and diuretics. Primaquine when combined into oral lipid nano-emulsion presented effective Anti-malarial activity against Plasmodium.

***3. Topical Delivery*:** The nano-emulsions can achieve a level of topical antimicrobial activity that has only been achieved by systemic antibiotics. The nano-emulsions have board spectrum activity against bacteria and fungi. The use of nano-emulsions in transdermal drug delivery represents an important area of research in drug delivery, which enhances the therapeutic efficacy and bioavailability of the drugs.

***4. Ocular Delivery*:** For the treatment of eye diseases, drugs are essentially administered topically. O/W Nanoemulsions have been investigated for ocular administration, to dissolve the poorly soluble drugs, to increase absorption and to attain prolong release profile. Nanoemulsions increases the contact time of the drug in the eyes, this may increases the bioavailability and reduces the need for frequent administration leading to improved patient compliance.

***5. In cancer therapy and targeted drug delivery in Nano emulsion*:** Another interesting application for the Nano emulsion formulations is the controlled and targeted drug delivery. Because of their submicron size, they can easily be targeted to the tumor area. The development of magnetic Nano emulsions is the innovative approach for cancer therapy.

***6. Pulmonary Drug Delivery*:** It is reported that cationic submicron emulsion can be considered as a promising carrier for DNA vaccines to the lung since they are capable to transfect pulmonary epithelial cells, which in turn induces cross preparing of antigen-presenting cells and directly activate dendritic cells, resulting in stimulation of antigen-specific T- cells. Therefore nebulization of submicron emulsions will be a new and coming research area.

***7. In Cosmestics*:** Nanoemulsions are used in cosmetics because there is no inherent creaming, sedimentation flocculation, that are observed with macroemulsion. Due to the lipophilic interior, nanoemulsions are suitable for the transport of lipophilic drug than liposomes and it support the skin penetration of active ingredients and thus increases their concentration in the skin.

***8. Antimicrobial Nanoemulsions*:** are O/W droplets and their size ranges from 200-600 nm. They are made by oil and water and are stabilized by surfactant and alcohol. The antimicrobial nanoemulsins has a broad spectrum of activity against bacteria like E.coli, Salmonella; viruses like HIV, Herpes simplex,etc. When nanoparticles fuses with the

pathogens, they release part of the energy trapped within the emulsion and which destabilize the pathogen lipid membrane, resulting in cell lysis and death.

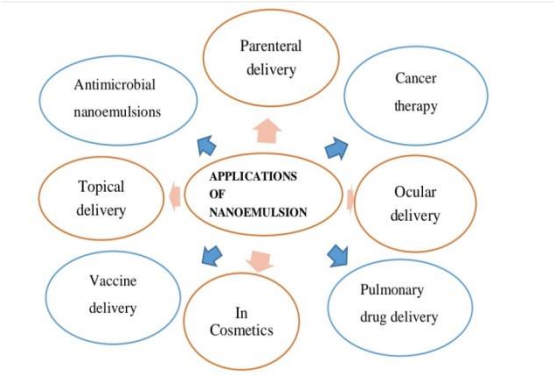

Fig. Different Applications of Non-aqueous Nano-emulsion.

CONCLUSION

Non-aqueous nano emulsion formulations are advantageous for the delivery of poorly water soluble drugs. Non aqueous nano-emulsion drug delivery system optimizes the performance of a wide spectrum of products and processes hence have attracted a great deal of attention. Many problems such as dealing with children or the elderly for whom pill swallowing can be difficult or even hazardous, unpleasant taste of water solution of drug and instability drug of in the presence of water or insolubility in water makes non aqueous nano-emulsion suitable for poorly aqueous soluble drugs. Non-aqueous nano-emulsions, drug delivery system, offer several merits for effective drugs delivery, biological, or diagnostic agents. Non-aqueous nanoemulsion technology can protect labile drug, increase bioavailability, enhances drug solubility and control the release of the drug. In this review article, Nanotechnology based drug delivery system, i.e. Non-aqueous nano-emulsion, has been presented with the efforts that they can serve as the building blocks for much more success in the field.

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