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A Review on Non -Aqueous Nano Emulsion

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Abstract

Generally emulsions are water-in-oil or oil-inwater type, but emulsions may contain polar liquid as one of the phase. Non-aqueous nano-emulsions are useful in many situations where presence of water is not desirable, and formulation of active ingredients which undergo hydrolysis or oxidation in the presence of water. The non-aqueous nano emulsion subject to design a stable non-aqueous nanoemulsion (NANE) using cosmetically approved ingredients as a vehicle for thewater-sensitive active ingredients. Non-aqueous nanoemulsion subject to increase the dermal penetration and permeation and study solubility and dermal bioavailability of drug. For better compliance, the non-aqueous nano emulsions will be incorporated in cosmetics or personal care products. A non-aqueous system was obtained with glycerin and olive oil stabilized by glycerol monosterate with co-surfactant. It was observed that emulsification behavior is completely unpredictable and conventional theories of emulsification and HLB system cannot be applied here. An optimized non-aqueous nano-emulsion is obtained through implementation of pseudo- ternary phase curve. Non-aqueous nano-emulsion region is determined and further characterized for pH, rheology, globule size analysis, zeta potential and stability. **[1]**

Keywords: Non-aqueous nano emulsion, HLB, Pseudo-ternary phase curve, ZetaPotential. [2]

Introduction

The non-aqueous nanoemulsion (NANE) useful for drug delivery and principally overcomes the problem of slow and incomplete dissolution of poorly water-soluble drugs with water unstable and/or unsavory drug. Emulsion is one of the most convenient and advantageous formulations in which one of the liquid phases is water; however, emulsion can be formulated without an aqueous phase to produce anhydrous, non-aqueous or oil-in-oil emulsions/microemulsion. Such systems can replace conventional emulsions where the presence of water has to be avoided. . Such systems can reduce the inherent limitations and facilitate the formation of solubilized phases from which absorption may occur. Unfortunately, the major difficulty in formulating NANE arises from the lack of appropriate data on surfactant action in relevant non-aqueous media, or indeed, the dearth of suitable surfactant designed for such specialized system.[3]

Non-aqueous nano-emulsions may be of pharmaceutical or cosmetic value if they are composed primarily of

edible, non-toxic ingredients and can be formulated to exhibit a wide range of physical properties. Some possible uses might be as topical application bases for dermatological, particularly for labile drugs, as emollient bases for cosmetic preparations, or

as nutrient preparations**[4]**

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.[5]

Disadvantages Of Non-Aqueous Nano Emulsion

1. Surfactants/co-surfactants concentration required for stabilization of nano-emulsions may bemore 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.**[6]**

Emulsion: An emulsion may be defined as a biphasic 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, the emulsifier is added to stabilize the system.[5]

Types of Emulsion

1. Water-in-oil emulsion: A water-in-oil emulsion is the type of emulsions which the continuous phase is usually hydrophobic materials such as oil and the dispersed phase iswater. More than 95% of the crude oil

emulsion formed in the oil field are the W/O type. The W/O emulsions contain three substances such as; a solvent, a surfactant, and water.[7]

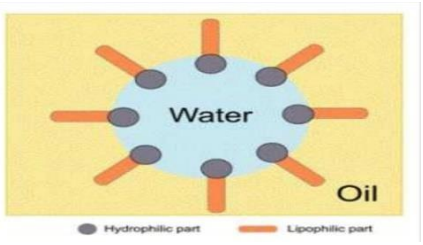

Fig.Water in Oil Emulsion

2. **Oil-in-water emulsion**: In oil in water emulsion oil droplets are dispersed throughout 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 are easily removable from the skin surface and they are used externally to provide cooling effect and internally to also mask the bitter taste of oil. Water soluble drugs are more quickly released from O/W emulsion. O/W emulsion give a positive conductivity test as water, the external phase is a good conductor of electricity.[9]

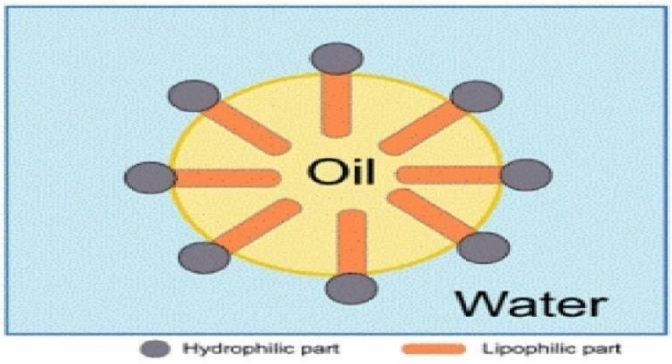

Fig.no.2. Oil in Water Emulsion

3. **Multiple emulsions:** Multiple emulsions are more complex than their two-phase counterparts from the standpoint of formulation, stability, and drug release. They are useful tool in achieving sustained release drug delivery for different routes. The present study aims towards formulation of multiple emulsions, which contain an additional reservoir that is an extra step for partitioning of the drug, which can effectively retard the release rate of the drug

and decrease the dose frequency.[10]

4. **Micro emulsion:** The term micro emulsion, also called as transparent emulsion, swollen micelle, micellar solution, and solubilized oil, was first used by Jack H. Shulman in 1959. Microemulsions are defined as thermodynamically stable, transparent (translucent) dispersions of oils and water that are stabilized by an interfacial film of surfactantmolecules.[12]

Biological Issues Or Drawbacks Of Non-Aqueous Systems

Very few biopharmaceutical studies have been performed with Non-Aqueous Systems, and there is a need for more comparative studies, particularly against solid dosage forms. However, it is worth speculating at this stage on the issues, which will influence the absorption from Non-Aqueous Systems. In case of oral drug delivery the rate of gastric emptying of Non-Aqueous Systems is similar to solutions, so that they are particularly useful where rapid onset of action is desirable. Conversely if the therapeutic index of the drug is low,

the rapid onset and accompanying high Tmax may lead to undesirable side effects**[7,8]**

Method of Preparation of Non-Aqueous Nano Emulsion

Various methods are used for the preparation of nanoemulsions including the high-energy and lowenergy emulsification methods and the combined methods are also used. Among the high- energy methods, the commonly used are high pressure homogenization, high-energy stirring and ultrasonic emulsification. Among the low- energy emulsification methods, the attention is focused on the phase inversion temperature method, the emulsion inversion point method and

the spontaneous emulsification method. **[9]**

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.[10]

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. [11]

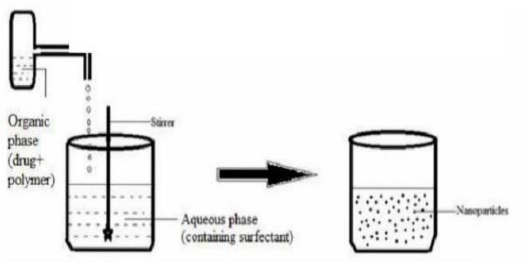

Fig.Solvent Displacement Technique

3. High-Shear Stirring .

In this method, high-energy mixers and rotor-stator systems are used for the preparation of nanoemulsions. Droplet sizes of the internal phase can be significantly decreased by increasing the mixing intensity of these devices. However, obtaining emulsions with the average droplet size less than 200-300 nm is rather difficult (Korelova & Yurtov, 2012). and pointed tips cause extreme shear and cavitation that result in breaking up of droplets. It has been observed that in most of the ultrasonic systems emitted sound field is inhomogeneous. For this reason, in order to have all droplets to experience highest shear rate, recirculation of the emulsion through the region of high power must be provided. Moreover, by doing this type of recirculation many times it is possible to obtain emulsions with uniform droplet size at dilute concentrations (Mason et al., 2006). [12,13]

***4. Phase Inversion Technique*:** This technique was based on the mechanism of changesof 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.[14]

5. Microfluidization

It is most widely employed in the pharmaceutical industry in order to acquire fine emulsions. In this method, a

device called microfluidizer is used which provides high pressures During the process, high pressure forces the macroemulsion to go through to the interaction chamberand thus nanoemulsions with submicron ranged particles can be produced. Uniform nanoemulsion production can be achieved by repeating the process many times and varying the operating pressure in order to get desired particle size (Chime et al., 2014; Jaiswal et al., 2015).**[15,16]**

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	PolyglycolizedGlycerides

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 dueto Brownian motion. Droplet size analysis of nanoemulsion can also be performed by

transmission electron microscopy (TEM).**[16,17]**

2. ***Viscosity Determination*:** The viscosity of nanoemulsion is measured by using Brookfield-type rotary viscometer at different shear rates at different temperatures.**[18]**

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.**[19]**

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.[20]

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.**[21]**

6. ***Refractive Index*:** Refractive index of nanoemulsion is measured by Abbesrefractometer.**[22]**

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 [23]

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. [24]

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. [25]

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.**[26]**

5. ***In cancer therapy and targeted drug delivery*****:** 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. [27]

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.[28]

***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. **[29]**

***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. **[30]**

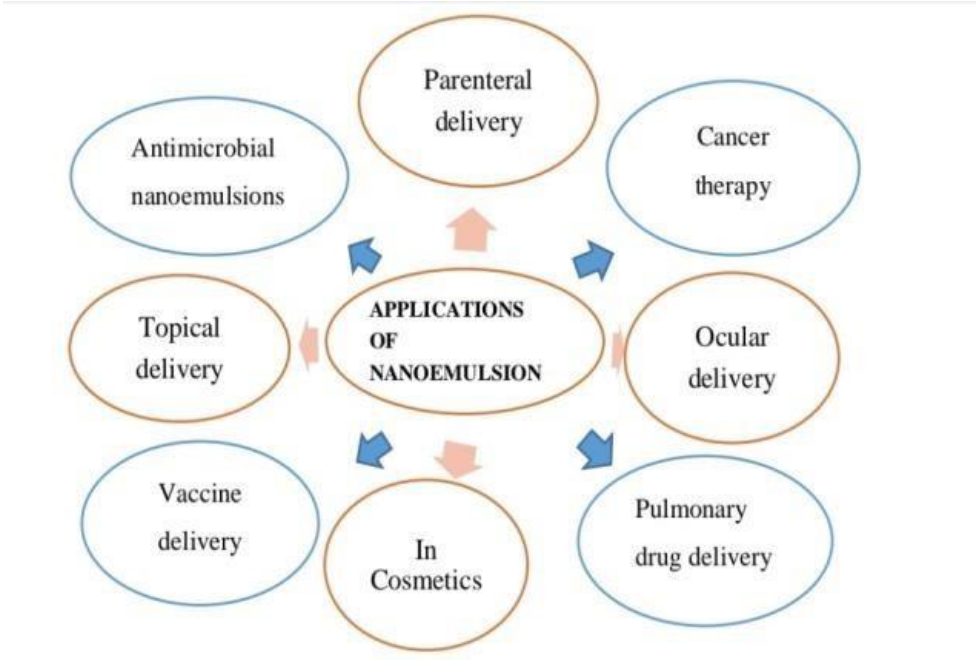

Fig. Different Applications of Non-aqueous Nano-emulsion

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 bedifficult 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. **[31,32]**

References.

1. S. Payghan, M. Bhat ,E. Toppo. Non-aqueous emulsion versatile vehicle For Drug Delivery, Article in pharmaceutical reviews, 2008.6.
2. A. Imhof, D.J. Pine. Stability of non-aqueous emulsions, Journal of colloid and interface science ,192, 368-374.
3. S. Roohinejad, R. Greiner,I. Oey, J.Wen.Emulsion based system for delivery of food active compound ,John Wilay ,2018, 1-4.
4. S. Roohinejad, R. Greiner, I. Oey, J.Wen.Emulsion based system for delivery of food active compound ,John Wilay, 2018,181-184.
5. O. Suitthimeathegorn.Intramuscular absorption and bio distribution of dexamethasone from non-aqueous emulsions in the rat, International Journal of Pharmaceutics,331(2),204-210.
6. C. Jadhav, V. Kate, S. Payghan. Investigation of effect of nonionic surfactant on preparation of griseofulvin non-aqueous emulsion.,Journal of Nanostruct Chemistry,2015,5, 107-113.
7. B. Khan, N. Akhtar, H. Khan, K. Waseem, T. Mahmood, A.Rasul, M. Iqbal, H. Khan. Basics of pharmaceutical emulsion:A review, African Journal of Pharmacy and Pharmacology,5(25), 2715-2725.
8. S. Akbari, A. Nour. Emulsion types, stability mechanisms and rheology: A review, International Journal of Innovative Research and Scientific Studies, 1 (1) 2018, 14-21.