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NANOEMULSION: A NOVEL CONCEPT FOR DRUG DELIVERY SYSTEM AND ITS CURRENT APPLICATIONS

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ABSTRACT

Nanoemulsions have small droplet size of 100 nm due to which it has large surface area per unit volume. The most important advantages of nanoemulsion are that it increases the solubility of the poor soluble drugs. In case of nanoemulsion problems like creaming, sedimentation and flocculation are removed. The destabilization in nanoemulsions generally occurs due to coalescence. The focus of this review article is on nanoemulsion and its current applications in various pharmaceutical fields.

KEYWORDS: Nanoemulsion, sedimentation, flocculation, destabilization.

INTRODUCTION

Nanoemulsions are considered as the emulsions whose droplet size is upto 100 nm. The basic compostion of nanoemulsion contain oil, water and an emulsifier. The main aim for the addition of emulsifier is that it decrease the interfacial tension between the oil and the water phases of the emulsion.[1]

Advantages of nanoemulsion

There are various advantages of nanoemulsion

- Good thermodynamic stability
- Better therapeutic effect compared to conventional formulations
- It can accommodate both hydrophilic and lipophilic drugs.[2, 3]

Factors affecting the Formulation of Nanoemulsion

1. Proper composition is used to avoid Oswald ripening.
2. The presence of excess surfactants enables new surface area of nanoscale to be rapidly coated during emulsification there by inhibiting induced coalescence.
3. Extreme share must be applied to rupture microscale droplets to nanoscale by providing the stress level to reach above the Laplace pressure of the droplets with a pressure of 10- 100 atm.

Theories of emulsification

According to the surface-tension theory, the interfacial tension between the two immiscible liquids is lowered by the addition of the emulsifiers or stabilizers. The oriented-wedge theory is based on the presumption that certain emulsifying agents orient themselves around a liquid droplet in a manner reflective of their solubility in that particular liquid. The plastic-or interfacial-film theory describes that the emulsifying agent is located at the boundary between the water and oil, forming a thin film by being adsorbed onto the surface of the internal phase droplets. The film avoids the contact and subsequent coalescence of the dispersed phase will result in greater physical stability of the emulsion.

Types of nanoemulsions

Depending on composition

- O/W Nanoemulsions: oil droplets are dispersed in continuous water phase.
- W/O Nanoemulsions: water droplets are dispersed in continuous oil phase.
- Bi-continuous Nanoemulsions: water and oil are dispersed with each other.

In all three types of Nanoemulsions interphase is stabilized by a combination of surfactant/ cosurfactant.

Advantage of nanoemulsions

a) Nanoemulsion generally avoids the first pass hepatic metabolism.
b) It enhances the rate of absorption of drug.
c) It increases bioavailability of the bioavailability of the drugs which are lipophillic in nature.
d) It is used to reduce the interfacial tension.
e) Nanoemulsions in comparision with the macro emulsions have higher surface area.
f) They are generally non-toxic and non-irritant so can be easily applied to the skin and mucus membrane.
g) It is thermodynamically stable system.

Disadvantages of nanoemulsions

a) The nanoemulsion formulation is an expensive process because it requires special instrument for size reduction of droplets.
b) For the stabilization of nanodroplets a large amount of surfactants and cosurfactant are required.
c) The stability of nanoemulsion is generally influenced by environmental factors such as temperature.[4]

METHODS FOR PREPARATION OF NANOEMULSIONS

1. High Pressure Homogenization

In this method high pressure and high energy is generated in order to form low particle size nanoemulsion. During this process several forces like hydraulic shear, intense turbulence and cavitation act upon it to generate the small droplet size nanoemulsion. Inorder to reduce the problem of coalescence more surfactant are added and it also helps in reduction of surface tension (as shown in fig. no.1).

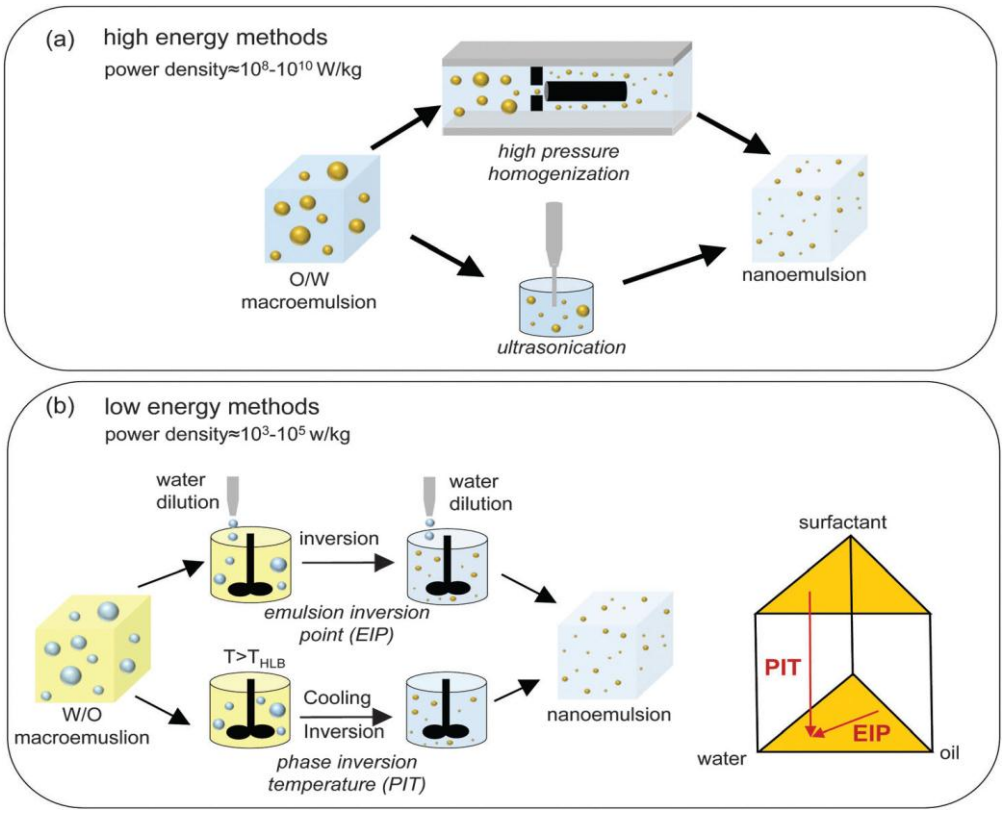

Fig. no.1: Overview of high energy and low energy methods for preparing O/W nanoemulsions.

2. Microfluidization

Microfluidization is a technique in which microfluidizer is used which uses high pressure positive displacement pump containing a small channels called microchannels. The product flows through these microchannels which results in a very fine particles. This technique can be used in the laboratory and industrial scale.

3. Phase Inversion Temperature Technique

In this method the phase inversion can be of two types: transitional inversion and catastrophic inversion.It is also used to reduce the particle size and produce stability against sedimentation or creaming with Ostwald ripening forming the main mechanism of nanoemulsion breakdown. This technique employs temperature dependent solubility of nonionic surfactants. This method consist of mixture of oil, water and nonionic surfactants which comprises of o/w microemulsions. when this microemulsion is completely heated then it leads to the phase inversion and for w/o emulsion.

4. Solvent Displacement Method

This method of nanoemulsion has been adopted from the nano precipitation method used for polymeric nanoparticles. In this the oily phase is dissolved in water-miscible organic solvents like ethanol and acetone. Then this organic solvent is poured into aqueous phase containing surfactant which leads to the formation of nanoemulsion by the rapid diffusion of organic solvent.

5. Phase Inversion Composition Method (Self-Nanoemulsification Method)

In this method nanoemulsion is developed at room temperature without the use of heat and organic solvent. In this technique stable nanoemulsion with droplet size of ~50 nm is obtained by the addition of water into the solution of surfactant in oil by continuous stirring at constant temperature.[4,5]

6. Ultrasonication

In this technique the reduce of particle size of nanoemulsion is done done with the help of ultrasonic sound frequency. The most important mechanism of this technique is the cavitation in which there is the change in intensity which leads to change in power density and hence reduce the particle size.[6]

EVALUATION PARAMETERS OF NANOEMULSION

1. Thermodynamic Stability Studies: The various formulations were subjected to different thermodynamic stability tests.
2. Droplet Size Analysis: The droplet size is analysed by photon correlation spectroscopy. In this the formulation is dispersed in 50 mL of water in a volumetric flask and gently mixed by inverting the flask.[7]
3. Transmission Electron Microscopy: Morphology and structure of the nanoemulsion usually determined by transmission electron microscopy (TEM).
4. Refractive Index: The refractive index, n, of a medium is defined as the ratio of the speed, c, of a wave such as light or sound in a reference medium to the phase speed, vp, of the wave in the medium represented by equation

$$n=c/vp - 1$$

It is determined using an Abbes type refractrometer.[7-8]

5. Drug Content: Drug content determine by reverse phase HPLC method using different columns of appropriate porosity.[8- 9]

RECENT APPLICATIONS OF NANOEMULSION

Nanoemulsions have unique properties which make it an attractive candidate for applications in the food, cosmetic, pharmaceutical industries and in drug delivery applications (as shown in fig. no. 3). Some of the properties of nanoemulsions are given below:

1. Plant Essential Oil Based Nanoemulsions

Recently in pharmacy essential oils are generally incorporated in the formulation of nanoemulsion to improve the aqueous solubility of lipophilic components, enhance oral bioavailability at reduced dosage concentration, provide good stability, transparency and also reduce toxic side effects by improving the biocompatibility.

a) Antioxidant activity

An ethanolic extract of local Phyllanthus urinaria, incorporated in palm kernel oil based nanoemulsion showed DPPH radical scavenging activity and could be used as a topical delivery for skin anti-ageing too.

b) Antimicrobial activity

Essential oil like Thymus daenensis produce nanoemulsion which is generally used ass antibacterial and also increase the ability A nanoemulsion of Thymus daenensis essential oil produced by high intensity ultrasound technique demonstrates superior antibacterial activity with increased ability to disrupt cell membrane integrity of a food-borne pathogen, E.coli.[7]

c) Anticancer activity

As of now, essential oils are investigated on glioblastoma, melanoma, leukemia and various cancers of oral, bone, breast, colon, cervix, kidney, liver, lung, ovary, pancreas, prostate and uterus cancers. In the recent decade, about hundred essential oils isolated from more than twenty plant families have been tested for more than twenty types of cancers.

d) Insecticidal and larvicidal activity

Citronella oil nanoemulsion shows decrease in release rates and thereby, enhances the mosquito protection rates.

2. Nanoemulsion in Food

Nanoemulsions can be used in the food industry to design smart foods with ingredients that are otherwise difficult to incorporate due to low-water solubility; an example is beta-carotene, a pigment responsible for color in vegetables like carrots possessing important health benefits. The possible application of nanoemulsions in improving the digestibility of food. The researchers showed that nanoemulsions prepared with circumin in the oil phase allow for easier digestion than when the circumin (as shown in fig. no. 2).[10]

3. Nanoemulsion in Cosmetics

The cosmetic formulation mainly faced problem of poor absorption of drugs through skin layers. With the help of nanotechnology and nanoemulsion, this problem can be resolve and absorption of cosmetic in skin is get stimulated due smaller droplet size. Recently the importance of nanoemulsions has become increasing as good vehicles for the controlled delivery of cosmetics and for the optimized dispersion of active ingredients in particular skin layers. Nanoemulsions are used for the transport of lipophilic drug and it also supports the skin penetration of active ingredients and thus increases their concentration in the skin.[11]

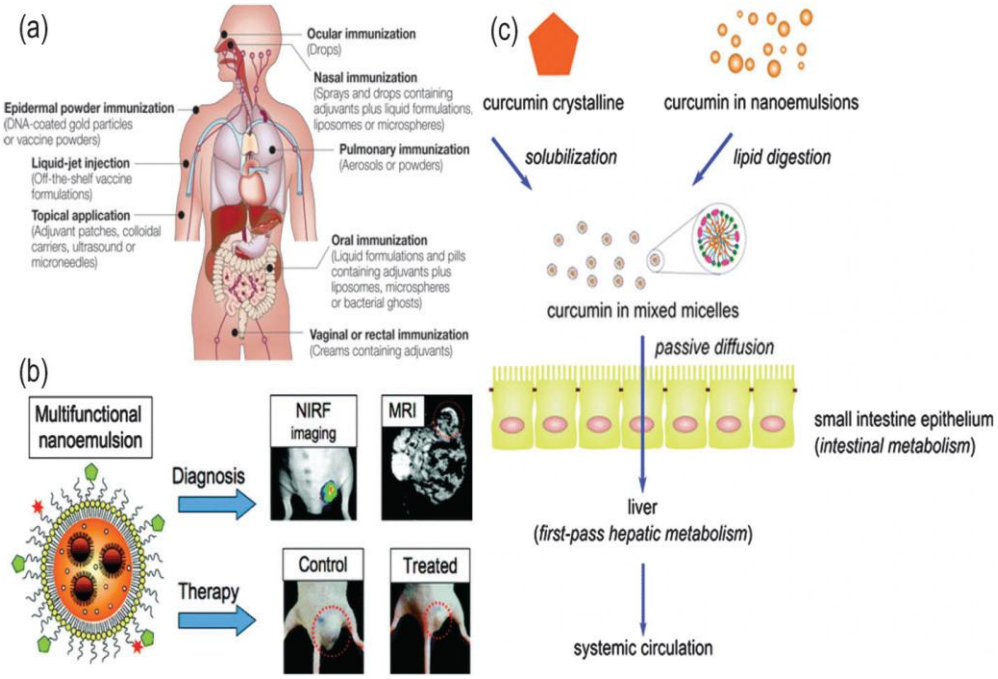

Fig. no.2: Nanoemulsions for applications in drug delivery and the food industry.
(a) Schematic of different modes of drug delivery in humans. (b) Magnetic nanoparticles added to nanoemulsions (c) Nanoemulsion with curcumin)

4. Nanoemulsions in cell culture technology

Nanoemulsions are a new method for the delivery of oil-soluble substances to human cell cultures. The system is based on a nanoemulsion that is stabilized by phospholipids. This nanoemulsion is transparent and can be passed through 0.1mm filters for sterilization. Nanoemulsions oil droplets are very easily taken up by the cells.[12]

5. Nanoemulsions in vaccines delivery

The nanoemulsion causes proteins applied to the mucosal surface to be adjuvant and it helps uptake by antigen presenting cells. This results in the significant systemic and mucosal immune response due to that the production of specific IgG and IgA antibody as well as cellular immunity.

6. Nanoemulsions in ocular and otic drug delivery

In order to increase the effectiveness of the drug, a dosage form should be chosen which increases the contact time of the drug in the eye. This may then increase the bioavailability, reduce systemic absorption, and reduce the need for frequent administration leading to improved patient compliance. So, nanoemulsions have been developed to overcome such problems.

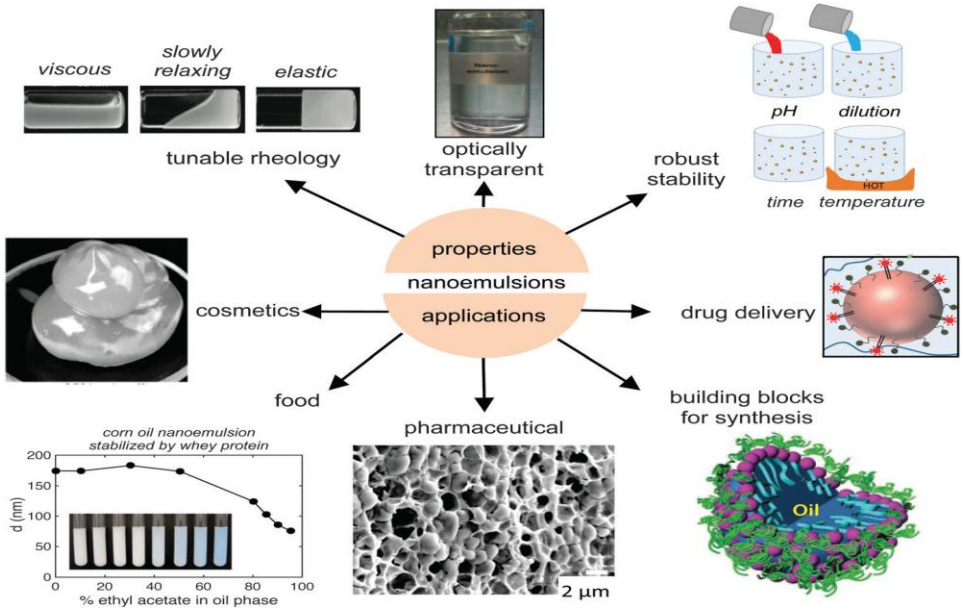

Fig no.3: Applications of Nanoemulsions.

CONCLUSION

Various recent patents on nanoemulsion and its formulation as been reported as shown in the table no.3. Nanoemulsions are used for targeted drug delivery of various anticancer drugs, photo sensitizers or therapeutic agents. Nanoemulsion can also provide prolonged action of the medicaments. Overall all nanoemulsion formulation may be considered as effective, safe and with increased bioavailability. Nanoemulsion has focused on various parameters to reduce the rate of Ostwald ripening. Nanoemulsion acts as a great supportive model system to enhance understanding of colloidal assembly and rheology of complex emulsion systems.

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