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Review Article

A Review on Nanoemulsions: Non-Toxic and Non-Irritant

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ABSTRACT

Nanoemulsions are nano-sized, spherical shape, clear transparent and translucent liquid and also known as miniemulsions, ultrafine emulsions, submicron emulsions. They have greater surface area due to small particle size (20-2000 nm) so owned kinetically stable. The thermodynamically unstable hydrophobic and hydrophilic drugs can be formulated as nanoemulsions. As the droplet size is so small, they are under constant Brownian motion and bluish appearance due to Rayleigh's scattering because wavelength of incident light is greater than droplet size. It may stabilized using amphiphilic surfactant that are biphasic dispersions. Nanoemulsions are used as non-toxic and non-irritant carriers for skin or mucous membrane through parenteral or non-parenteral administration in general and have been utilized in cosmetics. The toxicity caused by extreme amount of surfactant can be reduced by nanoemulsions. It can also be used for treatment of various diseases like HIV, and cancer. For reducing droplet size ultrasonic emulsification is very efficient. Sonicator probe provide the energy through sonotrodes in ultrasonic emulsification. Nanoemulsions require high pressure homogenization for their preparation.

1. Introduction

Nanoemulsions can be defined as oil-in-water (o/w) or water-in-oil emulsions with mean droplet diameters ranging from 50 to 100 nm. They are also known as sub-micron emulsions, miniemulsions, or ultrafine emulsions. These nanoemulsions are generally made up of two phases namely oily phase and aqueous phase. One of them is dispersed phase and another should be the dispersion phase.

Nanoemulsions are a group of dispersed particles used for pharmaceutical and biomedical aids and vehicles that show great promise for the future use in cosmetics, diagnostics, drug therapies and other biotechnologies. The small droplets of the nanoemulsions have the stability against the sedimentation or creaming with the Ostwald ripening which forms the main mechanism for the nanoemulsions breakdown. The internal structure of the nanoemulsions depends on the relative concentrations of components and other physical as well as chemical characteristics. Nanoemulsions form the domains of oil and water which are usually small (about 10-20 nm or less in diameter) so they do not scatter the light.

Nanoemulsions have the relative transparency and translucent properties. The shear of rheology was helpful to determine the flow properties. Nanoemulsions enhanced the shelf stability of themselves against the gravitational driven creaming. These nanoemulsions have wide applications but mainly they are used in treatment of various diseases, food and agricultural purposes, therapies, in cosmetics etc.

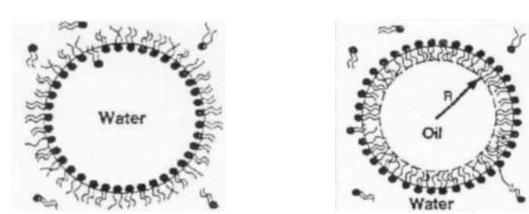

Fig 1. Types of Nanoemulsions

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These nanoemulsions are classified on the basis of composition of the oil and water present in them. Nanoemulsions are classified into three types:
Oil-in-water (o/w) nanoemulsions: These are the nanoemulsions in which the oil droplets are enclosed inside the continuous phase of water. O/w nanoemulsions are further classified according to the surfactants present as a) Anionic nanoemulsions b) Cationic nanoemulsions c) Neutral nanoemulsions.

In anionic nanoemulsions the anionic surfactant used are different soaps, sulfonates, and divalent ions. In cationic nanoemulsions the cationic surfactants are used. These includes different amines, quaternary ammonium compounds, and cetyl trimethyl ammonium bromide. In neutral nanoemulsions the neutral surfactants are used. The different polysorbates, fatty alcohols, esters, fatty acids are used as surfactants.

Water-in-oil (o/w) nanoemulsions: In this type of nanoemulsions the aqueous phase is enclosed in the oily phase which is continuous phase.

Bi-continuous nanoemulsions: In this type of nanoemulsions both oil phase and aqueous phase are inter-dispersed within the system in which they are formed.

2. Methods of preparation of nanoemulsions

2.1. High-energy methods (for lab and industrial preparation) for o/w & w/o emulsions

High-energy methods consume significant energy to make small droplets. To convert larger into smaller the stirring process is required at fast rate. It includes two steps:

Step-1: Production of oil in water macroemulsion by mixing oil, water and surfactant for a sufficient time period.

Step-2: Conversion of formed macroemulsion into a nanoemulsion.

2.1.1. High-pressure Homogenization

The high-pressure homogenization is also called as HPH. In this process macroemulsion is passed through a narrow gap through which larger droplets are broken into smaller droplets. The already prepared macroemulsions are passed through a narrow gap under high pressure. Then the larger droplets are converted into small droplets. This process can be repeated many times to get constant droplet size. In this method the pressure pump is useful to convert the larger droplets into smaller droplet. Using this method, the o/w nanoemulsions having less than 20% of the oil and extremely small particle size up to 1 nm can be prepared. The creamy nanoemulsions having the high viscosity or hardness whose particle size in less than 200 nm cannot be prepared by this method.

2.1.2. Microfluidization

Micro fluidization is the process in which the mixing of the particles at micron level is done by using the device called as microfluidizer. This is the patented technology. The fluids are forced to pass under pressure through the channels called as microchannels. The pressure required in this process is 500-2000 psi. These microchannels allow the mixing of the particles at the micro level. Then the two phases are passed through the microfluidizer. Microfluidizers are useful for producing different nanoemulsions having the distribution in their particle size. By using these methods kinematically and thermodynamically stable nanoemulsions are produced.

2.1.3. Ultrasonication

In this method high-energy shock waves are used to break the larger droplets into the smaller, so it is of better use than high-energy homogenizer. These high-energy shock waves provide the forces for the conversion of the macroemulsion to the nanoemulsion. This method is useful for the preparation of nanoemulsions containing drugs and foods. It can also be useful for loading the thermolabile drugs or molecules such as proteins, enzymes, nucleic acids, retinoids etc.

2.2. Low energy methods (lab preparation)

In this method low energy is required. The small droplets are formed without consuming the significant energy. The energy required for the process is 10^3 W per Kg.

This method includes two steps:

1) Preparation of w/o macroemulsion

2) Conversion of w/o into o/w nanoemulsion

2.2.1. Solvent diffusion method

Solvent diffusion method is a low scale method. In this method water soluble solvents such as acetone, ethanol and ethyl methyl ketone are used in which oily phase is dispersed. To yield the spontaneous nanoemulsion by the rapid diffusion of organic solvent, the organic phase is poured into aqueous phase. By using the process of vacuum evaporation, the organic solvent is removed.

2.2.2. Phase inversion method

Phase inversion method is an emulsification method. In this method the changes in surfactant is due to the temperature and the composition. The phase inversion method involves two methods: one is the transitional phase inversion method which involves phase inversion temperature (PIT) and phase inversion composition (PIC) and the second is catastrophic phase inversion (CPI) which involves the emulsion inversion. In this method as the temperature is taken constant the nanoemulsions having fine dispersions are produced.

3. Advantages of nanoemulsions

1. Nanoemulsions are thermodynamically and kinetically stable than the other emulsions.
2. Nanoemulsions have more penetration power and hence increases the absorption rate of drugs.
3. Eliminates the variability in absorption and also helps to solubilize lipophilic drugs.
4. Nanoemulsions are administered through oral, topical, parenteral, and ocular routes showing rapid and effective action.
5. Oil phase of nanoemulsion provides protection from the hydrolysis and oxidation of drug.
6. Nanoemulsions being liquids are convenient to patients and give the efficient effect without causing the adverse effects.
7. The physio-chemical stability of nanoemulsions can be increased by using the encapsulation of different food products.
8. Nanoemulsions are non-toxic and non-irritant in nature.
9. As the nanoemulsions are stable they do not harm the human body so it can be easily used in drug delivery system.

4. Nanoemulsions in different products

3.1. Nanoemulsions in food products

Nanoemulsions are used to prepare stable products. Certain bioactives have the low solubility but rapid metabolism which reduces its bioavailability whereas some are volatile and sensitive to changing conditions. These challenges can be overcome by using the nanoemulsions having the encapsulation of bioactive compounds. These nanoemulsions protect and prevent the food degradation for longer period of time. The plant oil has the antimicrobial activity against the pathogens but due to its hydrophobic property it cannot be directly used, so nanoemulsions are used for better application. In ice creams, the Unilever are used for reducing the fat content up to 16% present in it. Certain beverages contain nutrelease which are lipophilic compounds of β-carotene, omega-3, vitamins, phytosterols and isoflavones. The fresh and minimally processed foods are safely used by the application of the encapsulated natural antioxidants prepared from nanoemulsions.

3.2. Nanoemulsions in cosmetics products

Nanoemulsions are widely used in the cosmetic products. In response to the other cosmeceutical products these products penetrate deep into skin easily and give the fast effect. In facial powders, the talc powder, kaolin, iron oxide, and zinc oxide are present having the uniform particle size distribution which have effective stability and used as sunscreen protectants. These nanoemulsions are also used in moisturizers to improve the hydration of skin and prevent from getting dry. The nanoemulsions containing colours are used in lipsticks. L'Oreal is the nanoemulsion product containing cream which is used as an anti-wrinkle cream. Freeze 24/7 cream is also used as an antiwrinkle cream. The others examples are Caudalie, DDf acting as the antiaging creams and protect the skin from sun. Vitamin-E is used in the face cream to provide glow and healthy skin.

3.3. Nanoemulsions in herbal products

Nanoemulsions are used in herbal products to treat the defects naturally using ayurvedic medicines without any adverse effects. These herbal products are used as nanoemulsions in different products. Neem oil is used as an antibacterial, acaricidal as well as antifungal agent which is used in different soaps, facewashes, handwashes etc. Pilocarpine is also used in ocular retention as well as in treatment of glaucoma. The other examples are triptolide and clocetaxel which increase the hydration and acts as anti-inflammatory agents.

3.4. Nanoemulsions in vaccine delivery

Nanoemulsions containing vaccines have been researched and found to be effective and efficient for the treatment of various diseases. The influenza vaccine Arepanrix is prepared as nanoemulsion product which contain MF59 as an adjuvant. AS02 is the adjuvant used in the vaccine used for the treatment of malaria, HIV, and tuberculosis. The other examples are vaccines of leishmaniasis, and melanoma. By using the nanoemulsions in vaccine delivery it produces rapid effect.

3.5. Nanoemulsions in drug delivery system

Nanoemulsions are small in size and can be easily absorbed and easily eliminated through the body. Thus, they play an important role in improving the drug delivery system. There are different routes of drug administration such as oral, parenteral, ocular, topical.

Using these drugs, the bioavaibility of drug increases which enhances the drug delivery system. The oral delivery of drugs provides the non-irritant and non-toxic effect of drugs. The drugs are taken through the parenteral routes providing nutrition, supplementation required for the controlled drug delivery. Nanoemulsions are also used in anticancer treatment, vaccine delivery, antimicrobial diseases as well as viral diseases.

5. Conclusion

Nanoemulsions are emulsions that are extensively used in most of pharmaceutical systems and pharmaceutical industries. Formulations of these nanoemulsions give out several advantages of delivering drugs, biologicals, and diagnostic agents. They are mostly applied to almost all routes of delivery and also provide promising effect for many fields like therapeutics, many cosmetics and also biotechnology. In various targeted drug delivery systems, photosensitizers, and neutron capture therapy, the nanoemulsions are used as vehicles for administration. Nanoemulsions have wide range of applications in different areas like food industry, cosmetic industry, drug delivery systems, vaccine delivery as well as for the agricultural purposes. As the nanoemulsions have small size they are effectively useful for drug absorption as well as drug elimination. The non-toxic and non-irritant properties of nanoemulsions are making them more prominent carriers for delivering different categories of moieties as discussed in this review article.

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Conflict of Interest

The author(s) confirm that this article content has no conflict of interest.

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