



Review Article

NANO-EMULSION: A REVIEW ABOUT GENERAL INTRODUCTION, PREPARATION METHODS, EVALUATION AND SOME MARKETED NANOEMULSION FORMULATIONS

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Article Received on: 03/12/17 Approved for publication: 12/01/18

DOI: 10.7897/2230-8407.0913

ABSTRACT

Nano-emulsions are kinetically stable transparent nano-sized dispersions of oil-in-water (o/w) or water-in-oil (w/o) stabilized by an interfacial film of surfactant and co-surfactant. Due to their very small droplet size they are also known as sub-micron emulsion or mini emulsions. The efficacy of the nano-emulsion is enhanced by the nature and type of surfactant and co-surfactant which is employed in their formulation. This review specially focuses on the components used, advantages and disadvantages of nano-emulsions, methods of their preparation and few marketed preparations of Nano-emulsions.

Keywords: Nano-emulsion, submicron emulsion, mini emulsion, ultra-fine emulsion and characterization

INTRODUCTION

Nano-emulsion is a heterogeneous system composed of one immiscible liquid which is dispersed as droplet within another liquid. Droplet size of nano-emulsion generally ranges between 100 to 500nm. The size (diameter) and surface properties of the droplets is the key factor in biological activity of the nano-emulsion formulation. Small droplet size produces transparent/translucent nano-emulsion, so that the final appearance of the formulation is not affected when the oil phase is added. Nano -emulsions are spherical dispersed particles that are mainly used as pharmaceutical biomedical aids. Vehicles used, show a great promise for the future of cosmetics, diagnostics, drug therapeutics and biotechnologies¹. The term submicron emulsion², mini emulsion³ and Ultra Fine Emulsion⁴ are few synonyms used for nano-emulsions. From the studies it can be found that the nano-emulsion technology can be used for the bioavailability enhancement of lipophilic drugs⁵. In recent time nano-emulsion are frequently used for the delivery of various vaccines, DNA-encoded drugs⁶ and antibiotics⁷. Nano-emulsions are used in cosmetics and topical preparations also. Nano-emulsion can be delivered by various routes including oral, ocular⁸ and transdermal⁹. O/W type nano-emulsions were prepared long time ago, but W/O type nano-emulsion is recently investigated by K. Landfester¹⁰. Submicron sized nano-emulsions are very useful in overcoming the problems (e.g. poor bioavailability and non-compliance) that occur with the conventional delivery systems¹¹. The nano-emulsions can be used as drug carriers or as templates/molds/guides to produce nano-capsules.

ADVANTAGES OF NANO-EMULSIONS¹²

- Provides aqueous dosage forms for water insoluble drugs

- Helps in solubilizing lipophilic drugs
- Taste masking can be achieved
- Provides better bioavailability
- Both lipophilic and hydrophilic drugs can be incorporated within the same nano-emulsion formulation
- Improved drug efficacy
- Drug absorption variability can be reduced.

DISADVANTAGES OF NANO-EMULSIONS¹³

- Higher concentration of surfactant and co-surfactant is required for stability of the formulation and the surfactant to be used must be non-toxic.
- Nano-emulsion stability depends upon environmental parameters like temperature and pH.

SURFACTANTS USED

- Capryol 90
- Cremophor RH 100
- Lauroglycol 90
- Pleural oleique CC497
- Poloxamer 124 and 188
- Softigen 701 and 767
- Tagat T0
- Tween 8

COMPONENTS OF NANO-EMULSION

- Oil
- Surfactant
- Aqueous phase

LIST OF THE OILS USED IN THE NANO-EMULSION FORMULATION

- Glyceryl tricarylate/caprate
- Propylene dicaprylate/Dicaprate glycol
- Glyceryl tricaprylate
- Myristic acid isopropyl ester

PREPARATION METHODS^{15, 16}

Primary objective of nano-emulsion preparation is to achieve the droplet size range from 100-600 nm and another one is to provide stability conditions.

Nano-emulsion preparation require high energy amount which can be obtained with the help of mechanical equipment or by a chemical potential inherent.

Phase inversion method

In this method chemical energy resulting from phase transition through emulsification path is utilized to produce a fine dispersion.

Phase transition can be achieved by varying the composition at constant temperature or by varying temperature at constant composition. This method was developed by Shinoda et.al based on the changes in solubility of poly-oxy-ethylene type surfactant temperature.

With increase in temperature this surfactant becomes lipophilic but at lower temperature it forms oil-swollen micellar solution phase.

Sonication method

In this method the droplet size of ordinary emulsion or micro-emulsion is reduced by sonication method.

This method is not suitable for formulating larger batches of nano-emulsions.

High pressure homogenization

High pressure is applied over a system having oil phase, aqueous phase and surfactant or co-surfactant.

Homogenizer is used for pressure application.

CHARACTERIZATION OF NANO-EMULSION¹⁶**Particle size analysis**

Evaluation involves:

Hydrodynamic particle size

Particle size distribution

Dynamic light scattering method is used.

Surface charge measurement

- To predict the surface properties
- Surface zeta potential measurement with the help of mini electrode

Phase analysis

Measuring the electrical conductivity with the help of conductometer can be used to detect the type of emulsion (O/W or W/O).

Morphology

Sophisticated techniques e.g. x-rays, neutron scattering, atomic force microscopy, Cryo-electron microscopy are used to explore structure and behavior of nano-emulsions.

Viscosity¹⁷

Viscosity of nano-emulsion is a function of surfactant, water and oil components and their concentrations.

It can be measured by using a viscometer.

Increase in water concentration decreases the viscosity, while decreasing surfactant amount increases the interfacial tension between water and oil resulting in increased viscosity.

CONCLUSION

In comparison to micro-emulsions, nano-emulsions are kinetically stable and also require high energy methods for their preparation. Nano-emulsions have great advantages over the other conventional formulations but still there is very limited number of nano-emulsion formulations in the market till date. The preparation methods used for nano-emulsions are a bit costly, but with the increased interest in these formulations the cost is supposed to be reduced in future.

MARKETED NANO-EMULSION FORMULATIONS¹⁸

Drug/Bioactive	Brand Name	Manufacturer	Indication
Palmitatealprostadi 1	Liple	Mitsubishi Pharmaceutical, Japan	Vasodilator, platelet inhibitor
Dexamethason	Limethason	Mitsubishi Pharmaceutical, Japan	Steroid
Propofol	Diprivan	Astra Zeneca	Anesthetic
Flurbiprofenaxtil	Ropion	Kaken Pharmaceutical, Japan	NSAID
Vitamins A, D, E and K	Vitalipid	Fresenius Kabi Europe	Parenteral nutrition

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Cite this article as:

Arvind Kaur *et al.* Nano-emulsion: A review about general introduction, preparation methods, evaluation and some marketed nanoemulsion formulations. *Int. Res. J. Pharm.* 2018;9(1): 16-18
<http://dx.doi.org/10.7897/2230-8407.0913>

Source of support: Nil, Conflict of interest: None Declared

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