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Review Article

A REVIEW ON CURRENT TRENDS OF NANOEMULSIONShaikh Neha M.¹, Vijayendra Swamy S. M.¹, Nagoba Shivappa N.^{1*}, Shaikh Atiya L.¹¹Channabasweshwar Pharmacy College, Latur, Maharashtra, India.**Abstract:**

The Nanoemulsions have the potential in pharmaceutical industries because of the transparency at high droplet volume fraction, higher rate of bioavailability or diffusion and increased shelf life of the pharmaceuticals. Nanoemulsions are submicron sized emulsions that are under investigation as drug carriers for improving the delivery of therapeutic agents. These are clear, thermodynamically stable, isotropic liquid mixtures of oil, water, surfactant and co-surfactant. Reduction in droplet size to nanoscale leads to change in physical properties such as optical transparency and unusual elastic behaviour. Nanoemulsion droplet sizes are ranges from 20- 200nm and shows narrow size distribution. It is focused to give the brief regarding formulation aspect, evaluation parameters and various application of the nanoemulsions, several techniques are to be used for preparation of nanoemulsions like microfluidization, high pressure homogenization, low energy emulsification and solvent evaporation method and parameter that are to be used for its characterization like droplet size analysis, viscosity determination, drug content, refractive index, pH, zeta potential, SEM, Transmission electron microscopy, thermal stability, drug release and in vitro skin permeation study. Nanoemulsions have widespread applications in different fields such as pharmaceuticals, targeted drug delivery, food technology etc.

Key words: Nanoemulsion, Surfactant, Co-surfactant, High pressure homogenization, Emulsification.**Corresponding author:****Dr. Nagoba Shivappa N.**

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INTRODUCTION:

The drug delivery based on lipid formulations to improve the permeability and bioavailability of poorly water-soluble drugs. The choice of different novel drug delivery system has been used in which nanoemulsion plays an essential role in delivering the active pharmaceutical ingredient at the target organ or site. These are considered as an ideal alternative for improving the oral bioavailability of BCS (Biopharmaceutical drug classification system) Class II and IV drugs [1]. The Nanoemulsions are thermodynamically stable clear solution of two immiscible liquids, such as oil and water, stabilized by an interfacial film of surfactant molecules.

Nanoemulsions are novel drug delivery system includes an emulsified oil and water systems having mean droplet size which ranges from 50 to 1000 nm. The major difference between emulsion and nanoemulsion are; The nanoemulsions are thermodynamically and kinetically stable while emulsions are unstable. Emulsions are cloudy while nanoemulsions are clear and translucent. The emulsions and nanoemulsions differ mainly in the size and shape of the particles dispersed in continuous phase. The particle size in nanoemulsions is 10-200 nm and those of conventional emulsions are 1-20 μ m and formulation difference shown in fig.1 [2].

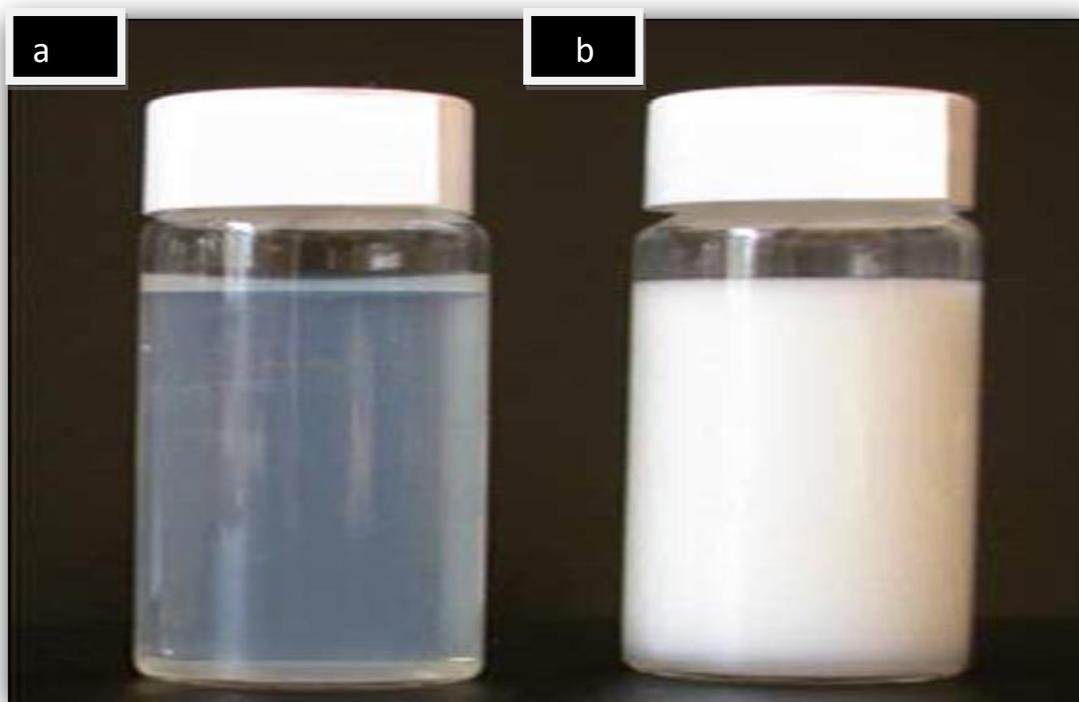


Fig.1; a -Nanoemulsions b- Microemulsion

Table.1- Difference in macroemulsion, microemulsion and nanoemulsion [3].

Parameters	Macroemulsion	Microemulsion	Nanoemulsion
Size	1-100 μ m	10-100 nm	20-500 nm
Shape	Spherical	Spherical ,lamellar	Spherical
Stability	Thermodynamically unstable, kinetically stable	Thermodynamically stable	Thermodynamically stable, kinetically stable
Method of preparation	High and low energy method	Low energy method	High and low energy method
Polydispersity	Often high (>40%)	Typically low (<10%)	Typically low (<10-20%)

TYPES OF NANOEMULSIONS:

Depends upon composition there are three types of nanoemulsions;

1. Oil in water (O/W): Nanoemulsions where oil droplets are dispersed in the continuous aqueous phase.
2. Water in oil (W/O): Nanoemulsions where water droplets are dispersed in the continuous oil phase.
3. Bi-continuous Nanoemulsions [4].

Advantages of Nanoemulsion over Other Dosage Forms

1. Increase the rate of absorption.
2. Eliminates variability in absorption.
3. Improve solubility of lipophilic drug.
4. Provides aqueous dosage form for water insoluble drugs.
5. Increases the bioavailability.
6. Various routes like topical, oral and intravenous can be used to deliver the product.
7. Rapid and efficient penetration of the drug moiety.
8. Helpful in taste masking.
9. Provides protection from hydrolysis and oxidation as drug in oil phase in O/W Nanoemulsion is not exposed to attack by water and air.
10. Liquid dosage form increases patient compliance.
11. Less amount of energy requirement.
12. Nanoemulsions are thermodynamically stable system and the stability allows self emulsification of the system whose properties are not dependent on the process followed.
13. Nanoemulsions can carry both lipophilic and hydrophilic drugs.
14. Nanoemulsions as delivery systems can improve the efficacy of a drug. [5]

Disadvantages of Nanoemulsion

1. A large concentration of surfactant and co-surfactant necessary for stabilizing the nanodroplets.
2. Limited solubilizing capacity for high-melting substances.
3. The surfactant must be nontoxic for using pharmaceutical applications.
4. Nanoemulsion stability is influenced by environmental parameters such as temperature and pH. These parameters change upon Nanoemulsion delivery to patients. [6]

Formulation additives of Nanoemulsion

Nanoemulsions are multiphase colloidal dispersion which is generally characterized by its stability and clarity. There is an application of high shear obtained by micro fluid or ultrasonic approach used to reduce

the droplet size to nanoscale. There is a marginal difference between the terms nanoemulsion and microemulsion. The microemulsion generally forms through thermodynamic self-assembly where as nanoemulsion requires external shear for rupturing the droplets. In retrospect, the historical choice of the word "microemulsion" to describe the nanoscale is unfortunate since they are structurally between 1 to 100 nm as for nanoemulsion. Microemulsions are not the emulsions of micro scale droplets. They are formed by self assembled equilibrium phase in which the surface tension does not play a significant role. The nanoemulsions underline the basic principle in its formulation. They generally comprise of two immiscible phase with an interfacial tension between them reduced by addition of surfactant. [7]

Following are the three main components of nanoemulsions:

1. Oil
2. Surfactant/Cosurfactant
3. Aqueous phase

1. Oil

Solubility of the drug in the oil phase is an important factor for the selection of oils. Specially this is very important in the case of oral formulation development, since the ability of nanoemulsion to maintain the drug in solubilized form is greatly influenced by the solubility of the drug in the oil phase. If the surfactant or cosurfactant is contributing to drug solubilization, there could be a risk of precipitation, as dilution of nanoemulsion in the gastrointestinal tract will lead to lowering of the solvent capacity of the surfactant or cosurfactant. In formulation of nanoemulsion various oils are used like Captex 355, Myritol 318, IPM, modified vegetable oils, digestible or non-digestible oils and fats such as olive oil, palm oil, corn oil, oleic acid, sesame oil, soybean oil, hydrogenated soybean oil, peanut oil and beeswax. Arachis oil (Peanut oil), Brahmi oil, Clove oil, Linseed oil (Flax seed oil), Eucalyptus oil, Peppermint oil, Neem oil, Tea tree oil, castor oil (Table 2). [8]

2. I) Surfactant

There are three types of surfactants used for stabilizing the systems. These are anionic, cationic, and nonionic. Nonionic surfactants are relatively less toxic than their ionic counter parts and typically have lower CMCs. Also, o/w nanoemulsion dosage forms for oral or parenteral use based on nonionic surfactants are likely to offer in vivo stability. Therefore, proper selection of surfactants becomes a crucial criterion. There are various types of surfactants shown in table 3. Another important criterion is the selection of surfactant with proper

HLB value. Hydrophilic surfactant and cosurfactant are considered to prefer the interface and to lower the necessary energy to form the nanoemulsions, consequently improving the stability. For example, the required HLB value to form o/w nanoemulsions should be greater than 10. The right blend of low and high HLB surfactants leads to the formation of a stable nanoemulsion upon dilution with water (Table 2 & 3). [9]

II) Cosurfactant

Cosurfactants are added to obtain nanoemulsion systems at low surfactant concentration. Short- to medium-chain length alcohols (C3–C8) are

commonly added as cosurfactants, which further reduce the interfacial tension and increase the fluidity of the interface. They also increase the mobility of the hydrocarbon tail and allow greater penetration of the oil into this region. Alcohols may also increase the miscibility of the aqueous and oily phases due to its partitioning between these phases. Therefore, ethanol, isopropyl alcohol, 1-butanol, and propylene glycol were selected as cosurfactants given in table 2. PEG 400 and Carbitol were also selected, as they also show increased permeation when incorporated into formulations and are relatively bearable.

Table 2; commonly used oils, surfactants and cosurfactants for the preparation of nanoemulsion. [10]

Sr.No	Oil	Surfactant	Cosurfactant
1.	Captex 355 (Glyceryl Tricaorylate/Caprates)	Capryol 90	Transcutol p
2.	Captex 200 (Propylene Dicaprylate/Dicaprate Glycol)	Tween 80	Glycerin, Ethylene glycol
3.	Captex 8000 (Glyceryl Tricaprylate) (Tricaprylin)	Lauroglycol 90	Propylene glycol
4.	Witepsol (90:10 % w/w c12 Glyceride tri: diesters)	PEG MW > 4000	Softigen 701, 767
5.	Myritol 318 (c8/c10 triglycerides)	Labrafil M 1944 CS, M 2125 CS	Ethanol
6.	Isopropyl myristate (Myristic acid isopropyl ester)	Poloxamer 124 and 188	Propanol

Table 3; Types of Surfactant [11-13]

Sr.No	Types of surfactant	Examples
1.	Non-ionic	Include polyoxyethylene surfactants such as Brij 35 (C12E35) or sugar esters such as Sorbitan monooleate (Span 80), Tween 80.
2.	Cationic	Ecithin preparations from a variety of sources including soybean and egg are available commercially and contain diacylphosphatidylcholine as its major constituent. Quaternary ammonium alkyl salts form one of the best known classes of cationic surfactants.
3.	Anionic	Sodium bis-2-ethylhexylsulphosuccinate (AOT) which is twin-tailed and is a particularly effective stabiliser of w/o microemulsions. Anionic surfactant is in common use consist of soap of Alkali, Amines, Metals, Sulphated alcohol and Sulphonates. Alkali Soap: Potassium and sodium stearate Amines Soap: Ethanolamine, Diethanolamine, Isopropanolamine, oleic acid Metals Soap: Calcium and aluminum stearate
4.	Ampholytic	Phospholipids are a notable example and exhibit excellent biocompatibility. At intermediate pH behave as Zwitterionic. Eg: Lecithin, N-dodocylalanine

3. Aqueous Phase

The droplet size and stability of nanoemulsion is influenced by the nature of aqueous phase. Hence,

pH and ionic content of aqueous phase should be given due importance while designing nanoemulsion. The physiological system has various pH ranges

varying from pH 1.2 (pH in stomach) to 7.4 and greater (pH of blood and intestine). It is well known that electrolytes can have influence on the nanoemulsion characteristics, such as droplet size and physical stability. Hence, it is advisable to evaluate the nanoemulsion and the characteristics of the resultant nanoemulsion in aqueous phases with varying pH and/or electrolyte concentration (depending upon the type of application). In addition to plain water, Ringer's solution, simulated gastric fluid (pH 1.2), simulated intestinal fluid (pH 6.8) and phosphate buffered saline can be used as aqueous phase to evaluate spontaneous nano emulsification of self-nano emulsifying drug delivery system. These studies indicate that the pH of the aqueous phase can have a great influence on the phase behavior of this system, especially when a drug with pH-dependent solubility is loaded in the system. [14]

FORMULATION METHODS OF NANOEMULSIONS:

The drug is being dissolved in the lipophilic part of the nanoemulsion i.e. oil and the water phase can be combined with surfactant and a cosurfactant is then added at slow rate with gradual stirring until the system is transparent. The amount of surfactant and cosurfactant to be added and the percent of oil phase that can be incorporated shall be determined with the help of pseudo-ternary phase diagram.

Construction Pseudo-ternary phase diagram

The purpose of pseudo-ternary phase diagram was to find out the concentration range of oil, surfactant and co-surfactant based on water uptake and the transparency of the formulation. The phase diagrams at surfactant: co-surfactant (S: COS) ratio (2:1 and 1:1), respectively. It was found that low percentage of oil (5%) was selected as the highest concentration to form stable nanoemulsion. 45% of S: COS mixture at a ratio (2:1) or (1:1) was selected as the minimum concentration for stable and successful nanoemulsion and as maximum safe concentration to prevent toxicity and irritation. It was reported that the highest flux and permeability coefficient was observed for a formulation that contains the maximum amount of

water, so 50% of the water was selected. The translucent nanoemulsion region is represented in phase diagrams with no observation of distinct conversion from water-in-oil (W/O) to oil-in-water (O/W) nanoemulsions.

Phase diagrams are obtained by mixing of the ingredients, which shall be pre-weighed into glass vials and titrated with water and stirred well at room temperature. Formation of monophasic/biphasic system is confirmed by visual inspection. In case turbidity appears followed by a phase separation, the samples shall be considered as biphasic. In case monophasic, clear and transparent mixtures are visualized after stirring; the samples shall be marked as points in the phase diagram. Several methods have been suggested for the preparation of nanoemulsion [15] i.e.,

1. High Pressure Homogenization

This technique makes use of high-pressure homogenizer/ piston homogenizer to formulate Nanoemulsion of extremely low particle size (up to 1 nm). During the process of homogenization, several forces, such as hydraulic shear, intense turbulence and cavitation, act together to yield Nanoemulsion with extremely small droplet size. High energy is required for the formation of small size (submicron) droplets. In nanoemulsion formulation several procedures are applied to increase the efficiency of emulsification. The emulsion is preferably prepared at high volume fraction of the disperse phase and diluted afterwards. However, very high phase volume ratios may result in coalescence during emulsification, but more surfactant could be added to create a smaller reduction in effective surface tension and possibly decrease recoalescence. Surfactant mixtures that show more reduction in surface tension than the individual components could also be used. If possible, the surfactant is dissolved in the disperse phase rather than the continuous phase; this often leads to smaller droplets. It may be useful to emulsify in steps of increasing intensity, particularly with emulsions having highly viscous disperse phase which shows in fig 2.

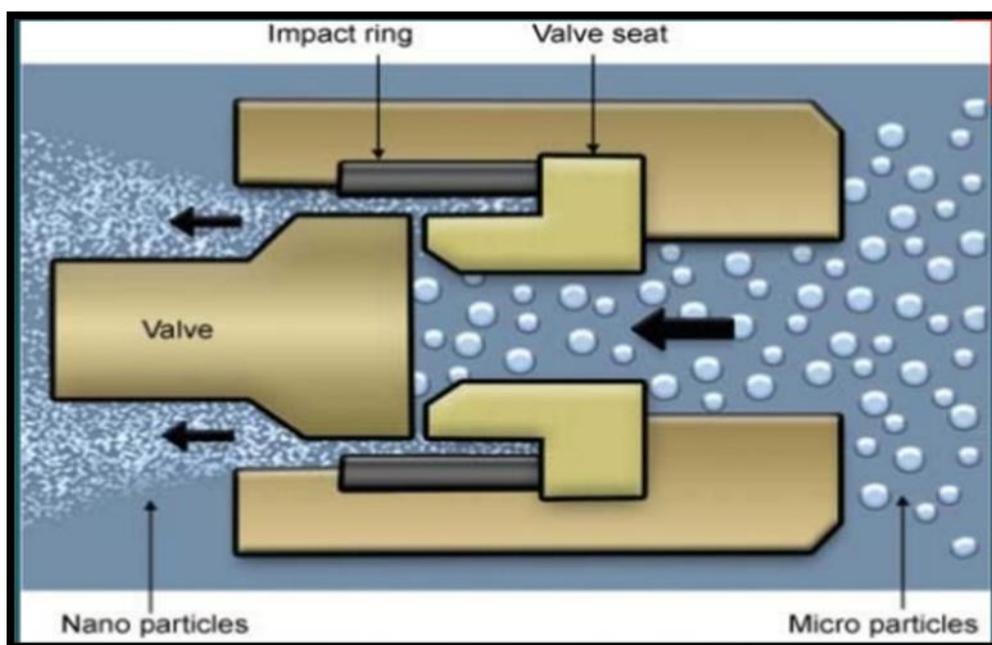


Fig.No.2 High pressure homogenization

2. Microfluidizer

In emulsion preparation higher pressure is used up to 700 Mpa, in the nozzle of microfluidizer that is the heart of this device (the interaction chamber) two jets of crude emulsion from two opposite channels collide with one another. The process stream is delivered by a pneumatically powered pump that is capable of pressurizing the in-house compressed air (150-650 Mpa) up to about 150 Mpa. The coarse emulsion is introduced into a microfluidizer where it is further processed to obtain a stable nanoemulsion. The

coarse emulsion is passed through the interaction chamber of the microfluidizer repeatedly until the desired particle size is obtained. The bulk emulsion is then filtered through a filter under nitrogen to remove large droplets resulting in a uniform nanoemulsion shown in fig 3. High- pressure homogenization and microfluidization can be used for fabrication of nanoemulsions at laboratory and industrial scale, whereas ultrasonic emulsification is mainly used at laboratory scale.

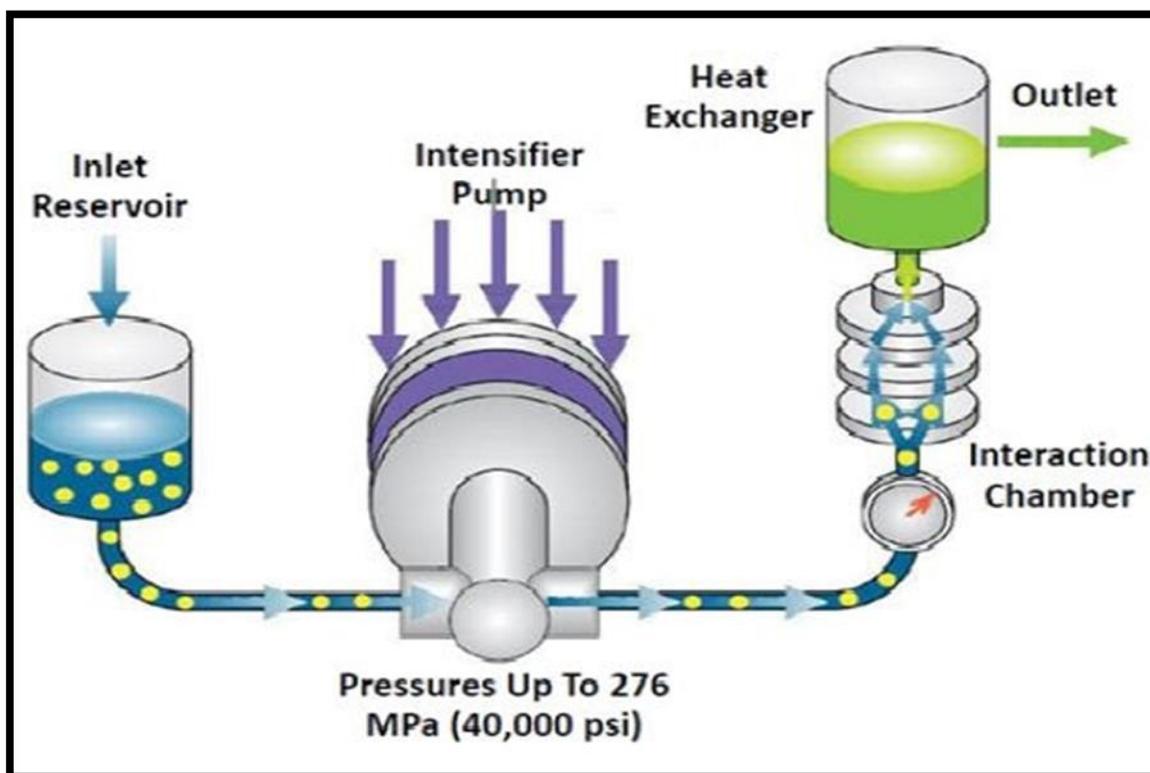


Fig .No.3 Microfluidizer

3. Phase Inversion Method

In this method, fine dispersion is obtained by chemical energy resulting of phase transitions occur through emulsification method. Fig.4 gives the adequate phase transitions are produced by changing the composition at constant temperature or by changing the temperature at constant composition. Phase inversion temperature (PIT) method was

introduced by Shinoda et al. based on principle of the changes of solubility of polyoxyethylene-type surfactant with temperature. This surfactant becomes lipophilic as increase in temperature because of dehydration of polymer chain. At low temperature, the surfactant monolayer has a great positive spontaneous curvature forming oil swollen micellar solution phase.

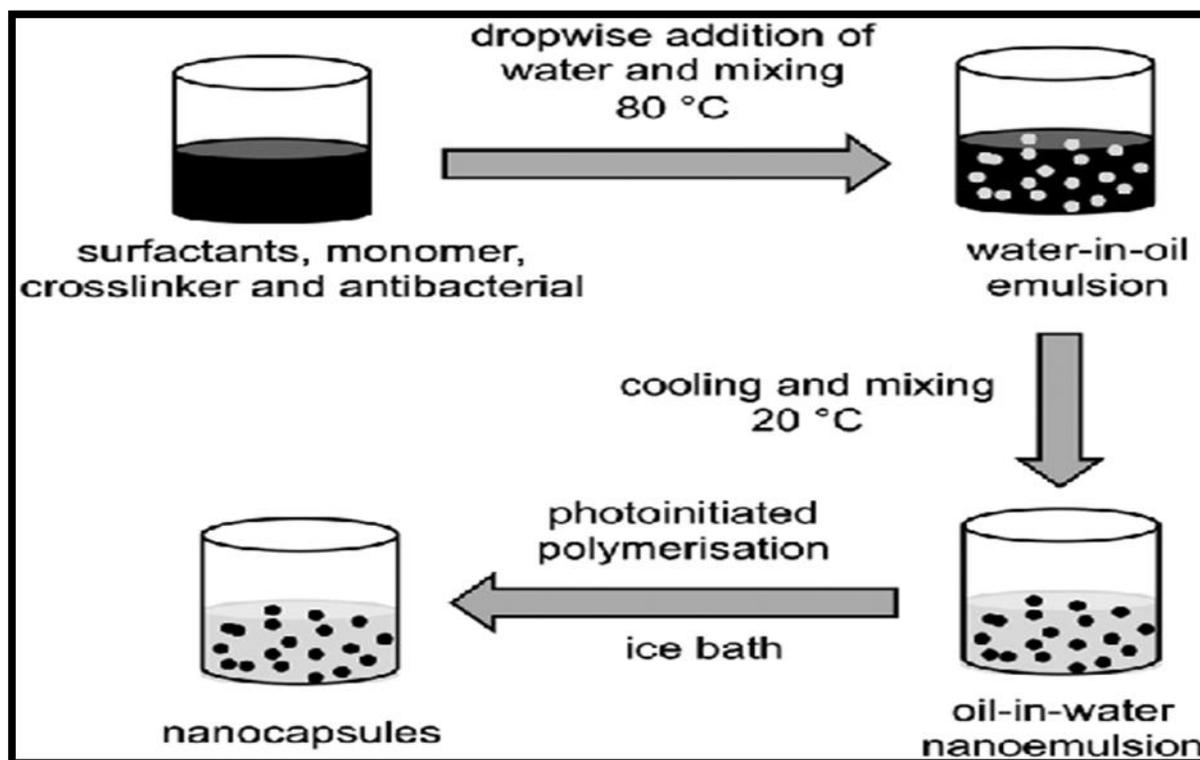


Fig.4.Phase inversion method

4. Solvent Displacement Method

The solvent displacement method for spontaneous fabrication of nanoemulsion has been adopted from the nanoprecipitation method used for polymeric nanoparticles. In this method, oily phase is dissolved in water-miscible organic solvents, such as acetone, ethanol and ethyl methyl ketone. The organic phase is poured into an aqueous phase containing surfactant to yield spontaneous nanoemulsion by rapid diffusion of organic solvent. The organic solvent is removed from the nanoemulsion by a suitable means, such as vacuum evaporation. Spontaneous nanoemulsification has also been reported when solution of organic solvents containing a small percentage of oil is poured into aqueous phase without any surfactant. Solvent displacement methods can yield nanoemulsions at room temperature and require simple stirring for the fabrication. Hence, researchers in pharmaceutical sciences are employing this technique for fabricating nanoemulsions mainly for parenteral use. However, the major drawback of this method is the use of organic solvents, such as acetone, which require additional inputs for their removal from nanoemulsion. Furthermore, a high ratio of solvent to oil is required to obtain a nanoemulsion with a desirable droplet size. This may be a limiting factor in certain cases. In addition, the process of solvent

removal may appear simple at laboratory scale but can pose several difficulties during scale up. [16]

5. Spontaneous Emulsification

It involves three main steps; Preparation of homogeneous organic solution composed of oil and lipophilic surfactant in water miscible solvent and hydrophilic surfactant. The organic phase was injected in the aqueous phase under magnetic stirring giving o/w emulsion. The water-miscible solvent was removed by evaporation under reduced pressure. [17]

CHARACTERIZATION OF NANOEMULSION:

1. Droplet size measurements

Size analysis of nanoemulsion was carried out by dynamic light scattering with zetasizer hsa 3000 (Malvern instruments Ltd., Malvern, U.K). Samples were placed in square glass cuvettes and droplet size analysis was carried out at Temperature 250 C, for 80 second duration.

2. Zeta potential measurements

Zeta potential for nanoemulsion was determined using zetasizer hsa 3000 (Malvern instrument Ltd., UK). Samples were placed in clear disposable zeta cells and results were recorded. Before putting the fresh sample, cuvettes were washed with the methanol and rinsed using the sample to be measured

before each experiment.

3. Transmission Electronic Microscopy (TEM)

Morphology and structure of the nanoemulsion were studied using Transmission Electron Microscopy (TEM) LEO 912AB EFTEM. To perform the TEM observations, samples were placed on a formvar carbon-coated copper grid (200 mesh in1) and then stained with 1% phosphotungstic acid. The excess phosphotungstic acid on the sample was gently wiped off using filter paper and examined after drying for about half an hour at room temperature.

4. Stability

i) Temperature stability

Shelf life as a function of time and storage temperature was evaluated by visual inspection of the nanoemulsion system at different time period. Nanoemulsion is diluted with purified distilled water to determine the temperature stability of samples. Samples are kept at three different temperature ranges (4°C, room temperature) and observed for any evidences of phase separation, flocculation or precipitation.

ii) Centrifugation

In order to estimate metastable systems, the optimized nanoemulsion formulation was diluted with purified distilled water. Then nanoemulsion is centrifuged at 10,000 rpm for 30 minute at room temperature and observed for any change in homogeneity of nanoemulsions. [18]

5. pH Determination

The pH of the prepared formulations is determined by pH using pH meter. In this, the formulations are place in 250 ml beaker and immersing the pH meter into the formulation and record the readings. Same process is repeated for three times with same formulation.

6. Rheological investigation

The viscosity of the different nanoemulgel formulations is determined at 25°C using a cone and plate viscometer or Brookfield viscometer with appropriate spindle# and connected to a thermostatically controlled circulating water bath.

7. Spreading coefficient Spreadability

It is determined by apparatus which consists of a wooden block, which is provided by a pulley at one end. The spreadability is measured on the basis of 'Slip' and 'Drag' characteristics of nanoemulgels. A ground glass slide is fixed on this block. An excess of nanoemulgel (about 2 g) under study is placed on this

ground slide. The nanoemulgel is then sandwiched between this slide and another glass slide. A 1 Kg weight is placed on the top of the two slides for 5 minutes to expel air and to provide a uniform film of the nanoemulgel between the slides. By putting weight of 80 g, the time (in seconds) required by the top slide to cover a distance of 7.5 cm with the help of string attached to the hook is noted. [19]

A shorter interval indicates better spreadability, which is calculated by the formulae:

$$S=M.L/T$$

Where,

S=Spreadability,

M=Weight tied to upper slide,

L=Length of glass slides

T=Time taken to separate the slides completely from each other.

8. Dye Solubilisation

A water soluble dye is solubilized within the aqueous phase of the W/O globule but is dispersible in the O/W globule. An oil soluble dye is solubilized within the oil phase of the O/W globule but is dispersible in the W/O globule.

9. Dilutability Test

O/W Nanoemulsions are dilutable with water whereas W/O are not and undergo phase inversion into O/W Nanoemulsion.

10. Conductance Measurement

O/W Nanoemulsion where the external phase is water, are highly conducting whereas W/O are not, since water is the internal or dispersal phase. To determine the nature of the continuous phase and to detect phase inversion phenomena, the electrical conductivity measurements are highly useful. A sharp increase in conductivity in certain W/O Nanoemulsion systems was observed at low volume fractions and such behaviour was interpreted as an indication of a „percolative behaviour“ or exchange of ions between droplets before the formation of bicontinuous structures. Dielectric measurements are a powerful means of probing both structural and dynamic features of Nanoemulsion systems.

11. Dynamic Light-Scattering measurements

The DLS measurements are taken at 90° in a dynamic light scattering spectrophotometer which uses a neon laser of wavelength 632 nm. The data processing is done in the built-in computer with the instrument.

12. Polydispersity

The average diameters and polydispersity index of samples were measured by Photon Correlation Spectroscopy. The measurements were performed at 25°C using a He-Ne laser.

Viscosity measurement

The viscosity of Nanoemulsions of several compositions can be measured at different shear rates at different temperatures using Brookfield type rotary viscometer. The sample room of the instrument must be maintained at $37 \pm 0.2^\circ\text{C}$ by a thermobath, and the samples for the measurement are to be immersed in it before testing.

13. 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, v_p , of the wave in the medium. It was determined using an Abbes type refractrometer at $25 \pm 0.5^\circ\text{C}$. [20]

$$n = c/v_p$$

APPLICATIONS OF NANOEMULSIONS:

1. Parenteral Delivery

Nanoemulsions are advantages for intravenous administration, due to the strict requirement of this route of administration, particularly the necessity for the formulation droplet size lower than 1 micrometer. Parenteral (or Injectable) administration of nanoemulsion is employed for a variety of purposes, namely nutrition eg. Fats, Carbohydrates, Vitamins etc. . Nanoemulsions of natural oils (soybean, sesame and olive) with the non toxic surfactant Pluronic F-68 via ultrasound for parenteral feeding. Lipid nanoemulsion has been widely explored for parenteral delivery of drugs. Nanoemulsion formulations have distinct advantages over macroemulsion systems when delivered parenterally because of the fine particle Nanoemulsion is cleared more slowly than the coarse particle emulsion and, therefore, have a longer residence time in the body. Both O/W and W/O Nanoemulsion can be used for parenteral delivery.

2. Oral Delivery

Nanoemulsion formulations offer the several benefits over conventional oral formulation for oral administration including increased absorption, improved clinical potency and decreased drug toxicity. Therefore, Nanoemulsion have been reported to be ideal delivery of drugs such as steroids, hormones, diuretic and antibiotics. Pharmaceutical drugs of peptides and proteins are

highly potent and specific in their physiological functions. Primaquine when incorporated into oral lipid nanoemulsion showed effective antimalarial activity against Plasmodium berghei infection in mice at a 25% lower dose level as compared to conventional oral dose. Lipid nanoemulsion of primaquine improved oral bioavailability by the liver with drug concentration higher at least by 45% as compared with the plain drug.

3. Topical Delivery

Topical administration of drugs can have advantages over other methods for several reasons, one of which is the avoidance of hepatic first pass metabolism of the drug and related toxicity effects. Another is the direct delivery and targetability of the drug to affected area of the skin or eyes. The nanoemulsion can achieve a level of topical antimicrobial activity that has only been previously achieved by systemic antibiotics. The nanoemulsion has broad spectrum activity against bacteria (e.g. E.coli, S. aureus) fungi (e.g. Candida, Dermatophytes) .

4. Ocular Delivery

For the treatment of eye diseases, drugs are essentially delivered topically. O/W Nanoemulsions have been investigated for ocular administration, to dissolve poorly soluble drugs, to increase absorption and to attain prolong release profile. [20]

5. Transdermal delivery

Indomethacin a potent NSAID, the anti-inflammatory effects of true optimized nanoemulsion formulation were compared with marketed gel in carragenan induced paw edema in rats. The %inhibition value was significant for developed Nanoemulsion, so great potential for transdermal application of indomethacin. Nanoemulsions for transdermal delivery of celecoxib. Formulation which consisted of 2% celecoxib 10% oil phase (Sefsol 218 and Triacetin) 50% surfactant mixture (Tween 80 and Transcutol -P) and 40% wate. The anti-inflammatory effect and percent inhibition value after 24h administration was found to be high for nanoemulsion formulation (81.2%) as compared to celecoxib gel (43.7%) and nanoemulsion gel (64.5%). The in vitro- in vivo studies revealed a significant increase in the anti-inflammatory effects of aceclofenac nanoemulsion (82.2%) as compared to nanoemulsion gel formulation (71.4%) and conventional gel (41.8%). [21]

6. Nanoemulsion in Cancer Therapy

Nanoemulsions can be used as vehicle in cancer

chemotherapy for prolonging the rate of drug release after intramuscular and intratumoral injection (W/O systems). It also enhances the transdermal drug delivery due to increase in the transport of anti-cancer drugs via lymphatic permeation through the skin and it is also non-irritant system.

NOEMULSIONS AS NANOCARRIER:

The principle of nanocarrier is based on the idea that extremely small size of the nanoparticles can pass through the biological barriers. Nanocarriers are polymers, amphiphilic lipids or solid colloidal particles which enclose the targeted drugs. Some examples of nanocarriers are gold nanoparticles, ceramic nanoparticles, liposomes, solid lipid nanoparticles, polymer-drug conjugates and carbon nanotubes. There are several different techniques by which drugs can be enclosed in nanoparticles. Nanocarriers are engineered in such a way as it can evade the immunological response and deliver the drug to targeted tissues.²² Nanoemulsion system can be used as a means to prepare nanocarriers for entrapping the drug. Drugs can either be entrapped in nanocarriers or bound with the surface of nanocarriers. Various emulsification methods are being used to prepare the nanocarriers. Nanocarriers can even be used very effectively to deliver the drug crossing the Blood Brain Barrier (BBB). [23]

CONCLUSION:

Overall, we can conclude nanoemulsion formulation may be considered as effective, safe and patient compliance drug delivery of pharmaceutical products. One of the distinctive characteristics of the nanoemulsion technology is the relatively high percentage of total particle volume occupied by the internal hydrophobic oil core of the droplets. In future further research work and development will be carried out for clinical application of nanoemulsion formulation.

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