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A REVIEW ON NANOEMULSION DRUG DELIVERY SYSTEM

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ABSTRACT

In this present study was carried out formation, characterization, properties, and applications of Nanoemulsions are reviewed and summarized. Nanoemulsions have the potential in pharmaceutical industries because of the transparency at high droplet volume fraction. Higher rate of bioavailability or diffusion & increased shelf life of pharmaceuticals. Nanoemulsions are clear, thermodynamically stable, isotropic liquid mixtures of oil, water, surfactant,& co-surfactant. Nanoemulsions are submicron sized emulsion that is under extensive investigation as drug carriers for improving the delivery of therapeutic agents. Nanoemulsions as a part multiphase colloidal dispersion is a heterogeneous system composed of fine oil in water /water in oil dispersion with surfactant and co-surfactant having droplets cover in the size range of 20-600 nm and droplet diameter approximately in the range of 0.5-100 nm. This review mainly discussed about the importance of nanoemulsions over other dosage forms, preparation methods, characterization of nanoemulsions and applications.

INTRODUCTION[1,2]

The term Nanoemulsion "refers to a thermodynamically stable isotropically clear dispersion of two immiscible liquids , such as oil and water stabilized by an interfacial film of surfactant molecules. Nanoemulsion is considered to be a thermodynamically or kinetically stable liquid dispersion of an oil phase and water phase in combination with a surfactant. The dispersed phase droplet size is about 5 nm -200 nm and should have very low oil/water interfacial tension. Co-surfactant or co-solvent is used in many cases in addition to the surfactant ,the oil phase and water phase. Now-a -day ˆs nanoemulsions are frequently used for various purpose like delivery of vaccine, DNA encoded drug ,antibiotics ,cosmetic and topical preparations and can be administrated via various routes like oral, pulmonary ,ocular and transdermal etc.

Depending on its composition there are three types of nanoemulsions: o/w (oli in water), w/o (water in oil),multiple emulsion {o/w/o(oil in water in oil),w/o/w (water in oil in water)}. The major difference between emulsion and nanoemulsions are while Nanoemulsions are thermodynamically and kinetically stable ,emulsions are unstable .Emulsions are cloudy while nanoemulsions are clear and translucent. Emulsion require the large energy input while nanoemulsions are formed either with or without high energy input. Emulsions have smaller surface area to volume , less free energy than nanoemulsion. Emulsions requires high amount of surfactant as compared to nanoemulsion, for e.g. 20-25% surfactant is added in the preparation of emulsion but 5-10% surfactant is added in Nanoemulsion. Ostwald ripening is the main mechanism of nanoemulsion breakdown.

Three types of Nanoemulsions[3] are most likely to be formed depending on the composition:

1.Oil in water Nanoemulsions where in oil droplets are dispersed in the continuous aqueous phase ;

2. Water in oil Nanoemulsions where in water droplets are dispersed in the continuous oil phase;

3. Bi-continuous Nanoemulsions where in microdomains of oil in water are interdispersed within the system.

The key difference between emulsion and nanoemulsions are that the former , whilst they may exhibit excellent kinetic stability ,are fundamentally thermodynamically unstable and will eventually phase separate. Another important difference concerns their appearance ; emulsions are cloudy while nanoemulsions are clear or translucent .In addition, there are distinct

differences in their method of preparation ,since emulsion require a large input of energy while nanoemulsions.

Fig.1. Nano-emulsion (left) with dia 35nm and a macro-emulsion (right) with dia 1μm

Advantages of Nanoemulsion over other dosage forms [4]:

1.Increase the rate of absorption.

2.Eliminates variability in absorption .

3.Helps in solublizing lipophilic drug .

4.Provides aqueous dosage form for water insoluble drugs .

5.Increases bioavailability .

6.Various routes like tropical ,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 dependant on the process followed.

13.Same Nanoemulsions can carry both lipophilic and hydrophilic drugs.

14. The use of Nanoemulsion as delivery systems can improve the efficacy of a drug , allowing the total dose to be reduced and thus minimizing side effects.

Disadvantages of Nanoemulsion Based Systems[5]:

1. Use of 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.

Theory of the Formation of Nanoemulsion [6]:

In Nanoemulsion which is categorized as multiphase colloidal dispersion which is generally characterized by its stability and clarity. There is an application of high shear generally obtained by micro fluid or ultrasonic approach generally used to reduce the droplet size to nanoscale. There is a marginal difference between the terms Nanoemulsion and microemulsion also known as micellar phase or mesophase .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 "micro-emulsion" to describe the nanoscale is unfortunate since they are structurally between 1 to 1000 nm as for Nanoemulsion. Microemulsions are not the emulsions of micro scale droplets. They are formed by self assembled equations phase in which the surface tension does not play a significant role. The generally comprises of two immiscible phase with an interfacial tension between them reduced by addition of surfactant.

Components of Nanoemulsion[7]:

1. Oil
2. Surfactant/Co-surfactant
3. Aqueous phase

1] Oils:-

Solubility of the drug in the oil phase is important criterion for the selection of oils This is particularly important in the case of oral formulation development ,as the ability of the 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 co-surfactant is contributing to drug solubilization

,there could be a risk of precipitation ,as dilution of nanoemulsion in GI tract will lead to lowering of the solvent capacity of the surfactant or co-surfactant.

Eg; 1. Captex 355

2. Captex 200
3. Captex 8000
4. Witepsol
5. Isopropyl Myristate

2] Surfactant:-

Solutes or molecules that are preferentially adsorbed at the surface or interface of liquids reduce the surface or interfacial tension and are therefore termed as surface active agents or surfactants.

Classification of Surfactants:

Depending on their ionization in aqueous solutions, surfactants can be classified as anionic ,cationic, non –ionic and amphoteric.

1. Anionic Surfactants: Anionic surfactant in common use consist of the soap of alkali, amines and metals, sulphated alcohols and sulphonates.

   Eg: Alkali soaps-potassium and sodium stearate.

   Amine soaps-ethanolamine , diethanolamine, iso-propanolamine, oleic acid.

   Metallic soaps-calcium and aluminium stearate.

2. Cationic Surfactants:

   Eg: Quaternary ammonium compounds such as cetrimide, benzalkonium chloride, benzethonium chloride.

3. Ampholytic Surfactants:

   Ampholytic surfactants are substances whose ionic characteristics depend on the pH of the system .At intermediate pH these behave as zwitter ions.

   Eg: Lecithin ,N-dodecylalanine.

4. Non-ionic Surfactants:

   The advantages of the these agents include their compatibility with both anionic and cationic surfactants, their resistance to pH change and effects of electrolytes and lower irritancy as compared to other surfactants.

   Eg: 1.Glycerol and glycol esters such as glycerol monostearate , propylene glycol monostearate.

2.macrogol esters such as polyoxyl stearates , polyoxyl- castor oil derivatives ,tweens (polysorbates)

Co-Surfactant:

Surfactant that acts in addition to another surfactant, further reducing the surface-tensions of the a liquid.

Eg: 1.Transcutol P

2. Ethylene glycol

3. Ethanol

4. Propylene glycol

5.Propanol

Factors affecting the Formulation of Nanoemulsion[8]:

- Appropriate composition is required to avoid Oswald ripening the dispersed phase should be highly insoluble in the dispersed medium.
- The surfactant is an essential part of the Nanoemulsion. They should not form lyotropic liquid crystalline "micro-emulsion" phases .Systems containing short chain alkenes , alcohols ,water ,and surfactants form the phases which are generally used with the co-surfactant.
- The presence of excess surfactants enables new surface area of nanoscale to be rapidly coated during emulsification there by inhibiting induced coalescence.
- Extreme share must be applied to rupture microscale droplets to nanoscale by providing stress level to reach above the Laplace pressure of the droplets with a pressure of 10-100 atm. Out of various methods ultrasonification is widely used in laboratory.

Techniques of Preparation of Nanoemulsions[9,10]:

Nanoemulsions are made from surfactants approved for human consumption and common food substances that are 'Generally Recognized as Safe' by the FDA . These emulsions are easily produced in large quantities by mixing a water- immiscible oil phase into an aqueous phase with a high –stress, mechanical extrusion process that is available worldwide.

Since nanoemulsions have very small particle size range , they can be most effectively produced using high-pressure equipment. The most commonly used methods for producing

nanoemulsions are 'High –pressure homogenization' and 'Micro-fluidization ' which can be used at both laboratory and industrial scale.

Other methods like 'Ultrasonification' and 'Spontaneous emulsification are also suitable but are mostly used at laboratory scale and not for commercial production.

1. High Pressure Homogenization:

This technique makes use of high-pressure homogenizer/ piston homogenizer to produce nanoemulsions of extremely low particle size (up to 1nm).In a high –pressure homogenizer ,the dispersion of two liquids (oily phase and aqueous phase) is achieved by forcing their mixture through a small inlet orifice at very high pressure 500 to 5000 psi),which subjects the product to intense turbulence and hydraulic shear resulting in extremely fine particles of emulsion.

Homogenizers of varying design are available for lab scale and industrial scale production of nanoemulsions . This technique has great efficiency ; the only disadvantage being high energy consumption and increase in temperature of emulsion during processing.

2. Microfluidization:

Microfluidization is a patented mixing technology ,which makes use of a device called microfluidizer. This device uses a high –pressure positive displacement pump (500-20000psi) , which forces the product through the interaction chamber ,which consists of small channels called 'microchannels' .The product flows through the microchannels on to an impingement area resulting in very fine particles of sub-micron range.

Method

The two solutions (aqueous phase and oily phase) are combined together and processed in an inline homogenizer to yield a coarse emulsion .The coarse emulsion is 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 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.

3. Spontaneous Emulsification:

The methodology for obtaining emulsions by spontaneous emulsification process three Steps:

- Preparation of the homogeneous organic solution composed of oil and a lipophilic surfactant in water- miscible solvent .The homogeneous aqueous phase was formed by water ,and hydrophilic surfactant. The organic phase was injected in the aqueous phase under magnetic stirring ; the o/w emulsion was formed instantaneously by diffusion of the organic solvent in the external aqueous phase leading to the formation of nanodroplets. The magnetic stirring was maintained during 30 min to let the system reach equilibrium.
- The totality of the water-miscible solvent was removed by evaporation during 45 min under reduced pressure. Nanodroplets of oil were dispersed in an aqueous solution of water and hydrophilic surfactant.

4. Phase inversion method:

In this method, fine dispersion is obtained by chemical energy resulting of phase transitions produced by emulsification pathway. The phase transition is produced by varying the composition of the emulsion and keeping temperature constant or vice versa. The phase inversion temperature was first done by Shinoda et al. it was concluded that increase in temperature results in the chemical changes of polyoxyehylene surfactants by degradation of the polymer chain with the temperature.

5. Solvent Evaporation Technique:

This technique involves preparing a solution of drug followed by its emulsification in another liquid that is non-solvent for the drug. Evaporation of the solvent leads to precipitation of the drug. Crystal growth and particle aggregation can be controlled by creating high shear forces using a high-speed stirrer.

6. Ultrasonication:

The preparation of Nanoemulsion is reported in various research papers which aim to use the ultrasonic sound frequency for the reduction of the droplet size. Another approach is the use of a constant amplitude sonotrode at system pressures in excess of the ambient value .It is well known that increasing the external pressure increases the cavitations threshold within an ultrasonic field and thus fewer bubbles form .However , increasing the external pressure also increases the collapse pressure of cavitations bubbles. This means that the collapse of the bubbles when cavitation occurs becomes stronger and more violent than when the pressure is at

atmospheric conditions. As cavitation is the most important mechanism of power dissipation in a low frequency ultrasonic system, these changes in navigational intensity can be related directly to changes in the power density. The system also uses a water jacket to control the temperature to optimum level.

7. Hydrogel Method:

It is similar to solvent evaporation method. The only difference between the two methods is that the drug solvent is miscible with the drug anti-solvent. Higher shear force prevent crystal growth and Ostwald ripening.

Characterization of Nanoemulsion[11]:

The droplet size ,viscosity ,density ,turbidity , refractive index ,phase separation and pH measurements shall be performed to characterize the Nanoemulsion. The droplet size distribution of Nanoemulsion vesicles can be determined by either light scattering technique or electron microscopy. This technique has been advocated as the best method for predicting Nanoemulsion stability.

1.Dye Solubilization:

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.

2. Dilutability Test :

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

3. Conductance Measurement:

O/W Nanoemulsion where the external phase is water, are highly conducting where as 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 behavior was interpreted as an indication of a ‘percolative behavior ’ or exchange of ions between droplets before the formation of bi-continuous structures. Dielectric measurements are a powerful means of probing both structural and dynamic features of Nanoemulsion systems.

4. Dynamic Light –Scattering measurements:

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

5.Polydispersity:

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

6. Phase analysis:

To determine the type if Nanoemulsion that has formed the phase system (O/W or W/O) of the Nanoemulsions is determined by measuring the electrical conductivity using a conductometer.

7. Interfacial Tension:

The formation and the properties of Nanoemulsion can be studied by measuring the interfacial tension. Ultra low values of interfacial tension are correlated with phase behavior , particularly the existence of surfactant phase or middle –phase Nanoemulsions in equilibrium with aqueous and oil phases.

Spinning –drop apparatus can be used to measure the ultra low interfacial tension. Interfacial tensions are derived from the measurements of the shape of a drop of low-density phase ,rotating it in cylindrical capillary filled with high-density phase.

8. 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±0.2ºc by a thermo bath, and the samples for the measurements are to be immersed in it before testing.

9. pH

The apparent pH of the formulation was measured by pH meter.

10. Refractive Index:

The refractive index ,n, of a medium is defined as the ratio f the speed, c, of a wave such as light or sound in a reference medium to phase speed , vp , of the wave in the medium. n=c/vp; It was determined using an Abbes type refractometer at 25±0.5ºC.

11. Transmission Electron Microscopy(TEM):

Morphology and structure of the nanoemulsion were studied using transmission electron microscopy. Combination bright field imaging at increasing magnification and of diffraction modes was used to reveal the form and size of nanoemulsion droplets. Observations was performed as, a drop of the nanoemulsion was directly deposited on the holey film grid and observed after drying.

12. Thermodynamic stability studies: During the thermodynamic stability of drug loaded Nano-emulsions following stress tests as reported:

a. Heating Cooling Cycle: Nanoemulsion formulations were subjected to six cycles between refrigerator temperature (4ºc) and 45ºc .stable formulations were then subjected to centrifugation test.

b. Centrifugation: Nanoemulsion formulations were centrifuged at 3500 rpm and those that did not show any phase separation were taken for the freeze thaw stress test.

C .Freeze Thaw Cycle: In this the formulation were subjected to three freeze thaw cycles between 21ºc and +25ºc kept under standard laboratory conditions. These studies were performed for the period of 3 months.

APPLICATIONS OF NANOEMULSIONS :

1. Solubilization of poorly soluation ble drugs:

Solubilizatio of poorly soluble drugs is most apparent application for nanoemulsions. Eg: Lorazepam is injected intravenously for premedication and sedation before an operation. It is usually administered as a solution in organic solvents such as propylene glycol. The highest concentration that can be achieved in an aqueous diluents (5% dextrose in water) is 0.05 mg/ml. a phospholipids stabilized soybean oil emulsion was able to stably emulsify lorazepam at 1 mg/ml, a 20 – fold increase, which could significantly reduce the volume needed for injection.

2. Reduced pain/ irritation :

At the direct site of intravenous injection, some drugs can cause local irritation. These drugs, as well as certain co-solvents in aqueous solutions, can also cause phlebitis, an inflammation of a vein that can lead to pain or redness. Nanoemulsion eliminate the need for co-solvents, as well as encapsulating drugs that might otherwise be irritants, and in both cases can reduce local irritation upon injection.

3. Reduced toxicity of drug :

Beyond the site of injection, drugs or their delivery vehicles can also cause irritation or toxicity once in the body. Paclitaxel is an important chemotherapeutic agents used in the treatment of breast, ovarian, colon and non-small cell lung carcinomas. The commercially available product Taxoll 9 Bristol-Myers Squibb) is formulated in a 1:1 v/v mixture of ethanol and polyoxy ethylated castor oil (cremophore EL). Cremophore EL has been associated with bronchospasms, hypotension ,and other hypersensitive reactions. To reduce the toxicity associated with cremophore EL, incorporation of paclitaxel into a wide variety of drug delivery vehicles, including liposomes, micelles, emulsions and cyclodextrins, has been investigated. A representative nanoemulsion example will be described. For the commercially available taxoll formulation the Maximum Tolerated Dose(MTD) was approximately 20 mg/kg where as for the nanoemulsion formulation it was approximately 70 mg/kg , over three times greater. The efficacy of the nanoemulsion formulation was assessed with B16 melanoma, a fast growing solid murine tumor. Nanoemulsions showed increasing efficacy at increasing dosage amounts and were better than the commercial formulation in all cases.

5.Improved pharmacokinetics :

Pharmacokinetics is concerned with the fate of external substances introduced to the body, specifically the extent and rate of absorption, distribution, metabolism and excretion of compounds. Improving these parameters for more favourable drug performance is a primary objective of drug delivery research in general and for nanoemulsions specifically one specific parameter that will be mentioned multiple times is the area under the concentration time once, abbreviated AUC.

Eg: Nalbuphine is morphine like drug and once of its advantages over morphine is that it lacks significant withdrawal symptoms. However, due to its short elimination half-life and poor oral bioavailability it needs to be injected every 3-6 hours prodrugs of nalbuphine have been investigated for parenteral administration, and Fang and co workers sought to use Nanoemulsions for both nalbuphine and its prodrugs.

APPLICATIONS OF NANOEMULSIONS IN DRUG DELIVERY SYSTEMS:

1.Parenteral Delivery :

Nanoemulsion 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 administration of nanoemulsion is employed for a variety of purposes, namely nutrition eg. Fats, Carbohydrates,Vitamins etc. Nanoemusions of natural oils 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 macro-emulsion 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 bergheii 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 be 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 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 bacterial fungi.

4.Ocular Delivery :

For the treatment of eye diseases, drugs are essentially delivered topically.

O/W Nanoemulsion have been investigated for ocular administration, to dissolve poorly soluble drugs, to increase absorption and to attain prolong release profile.

5.In Cosmetic :

The aesthetic properties, i.e low viscosity and transparent visual aspects of nanoemulsion with droplet sizes below 200 nm, its high surface area allowing effective transport of the active ingredient to the skin make them especially attractive for their application in cosmetics. Nanoemulsionss are acceptable in cosmetics because there is no inherent creaming, sedimentation, flocculation or coalescence that are observed with macro-emulsion. The incorporation of potentially irritating surfactants can be avoided by using high energy equipment during manufacturing. Nanogel technology to create miniemulsion from oil-in water concentrate suited to minimizing transepidermal water loss, enhanced skin protection and penetration of active ingredient. It would be useful for sun care products, moisturing and antiageing creams. It helps to give skin care formulations a good skin feels.

6.Transdermal :

Indomethacin a potent NSAIDS, 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 10% oil phase 50% surfactant mixture and 40% water.

The anti-inflammatory effect and percent inhibition value after 24 h 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%).

7. In Biotechnology :

Many enzymatic and biocatalytic reactions are conducted in pure organic or aqua-organic media. Biphasic media are also used for these types of reactions. The use of pure a polar media causes the denaturation of biocatalysts. The use of water-proof media is relatively advantageous.

Enzymes in lower water content display and have-

- Increased solubility in non-polar reactants.
- Possibility of shifting thermodynamic equilibria in favour of condensations.
- Improvement of thermal stability of enzymes, enabling reactions to be carried out at higher temperatures.

Stability Factors of Nanoemulsion : As a general consideration the stability of nanoemulsion largely depends upon the following factors;

a] Coalescence of the two droplets of dispersed phase due to the surface tension and intermolecular attractions. This is mainly reduced by addition of suitable surfactants.

b] If the dispersed phase has high solubility in the dispersed medium. This results in diffusive migration of smaller droplets with low Laplace pressure to larger droplets of high Laplace pressure also known as Ostwald's ripening. The dispersed phase should be selected such that it should have minimum or no solubility in the continuous phase.

CONCLUSION

Nanoemulsions formulations offer several advantages for delivery of drugs, biological, or diagnostic agents. Traditionally, NEs have been used in clinics for more than four decades as total parenteral nutrition fluids. Several other products for drug delivery applications such as Diprivan, Liple and Ropion have also reached the market place. Although NEs are chiefly seen as vehicles for administering aqueous insoluble drugs, they have more recently received increasing attention as colloidal carriers for targeted delivery of various anticancer drugs, photo sensitizers neutron capture therapy agents, or diagnostic agents. Because of their submicron size, they can be easily targeted to tumor area. Recently, several research papers have been published for the improvement of drug delivery, but still there is a need to emphasis on its characterization part including in-vitro evalution. Besides this, research papers shows higher percentage of surfactant used for treatment of Nanoemulsion, irrespective of different routes of administration, but there is a lack of toxicological evaluation of the prepared Nanoemulsions, which can be a broad research area in future.

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