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Review Article

A Review on Nanoemulsion Based System

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ABSTRACT

Nanoparticles: - Targeted drug delivery system is a special form of drug delivery system where the medicament is selectively targeted or delivered only to its site of action or absorption and not to the non- target organs or cells. Nanoparticles were first developed by Birrenbach and Spiser and co-worker Kreuter in the year 1976. (1). Nanoemulsion: - Emulsion is a system containing two immiscible phases and composed of at least three components: water phase, oil phase and surfactant phase. The nature of the surfactant determines the continuous phase (external phase) of the emulsion. (6) Aim: - A Review on Nanoemulsion Based System. Objective: - The main objective of nanoemulsion is particle size reduction for the better absorption of drug. It increases the pharmacokinetic effect of the drug substance. With the help of nanoemulsion the drug will release in controlled manner. Nanoemulsion increases the safety profile of the drug. It helps to reduce the drug dosing and improve the bioavailability of drug. Result And Discussion: Nanoemulsion drug delivery technologies efficiently overcome the low bioavailability disadvantage associated with hydrophobic medicines and other pharmaceutical or chemical components with high first pass metabolism. Researchers have employed high energy technologies to improve the delivery of medications and other pharmacological or chemical components. high energy methods are more expensive than low energy methods, which require less energy and are more efficient. Because high energy methods require low surfactant concentrations. Furthermore, research papers show that a higher percentage of surfactant (much higher than CMC level) is used for the formation of Nanoemulsion, regardless of the route of administration, but there is a lack of toxicological evaluation of the prepared Nanoemulsion, which could be a broad research area in the future. Conclusion: Nanoemulsion formulations have various advantages for pharmacological, biological, or diagnostic agent administration. For more than four decades, NEs have been used as whole parenteral feeding fluids in clinics.

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Although Nanoemulsion are commonly used to provide aqueous insoluble medications, they have lately gained popularity as colloidal carriers for the targeted delivery of certain anticancer drugs, photosensitizes, neutron capture therapy agents, or diagnostic agents. They can be easily targeted to the tumor location due to their submicron size.

INTRODUCTION

Nanoparticles: - Targeted drug delivery system is a special form of drug delivery system where the medicament is selectively targeted or delivered only to its site of action or absorption and not to the non- target organs or cells. Nanoparticles were first developed by Birrenbach and Spiser and co-worker Kreuter in the year 1976.(1).

Emulsion: - Emulsions are metastable colloidal systems composed of one immiscible liquid dispersed in another. Emulsions are utilised in a variety of products, including paints, medications, cosmetics, food, and for improved oil recovery.(2).

Micro-Emulsion: - Micro-emulsions are liquid combinations of oil, water, and surfactant that are transparent, stable, and isotropic; they typically also contain a co- surfactant.(3). Besides that, micro emulsions have droplet sizes of the dispersed phase ranging from 10nm-100nm.(2).

Table No. 1: Property of Macro-emulsion, Nanoemulsion, Micro-emulsion. (6) (7).

Sr. No.	Property	Macroemulsion	Nanoemulsion	Microemulsion
1	Size	1-100 µm	20-500 nm	10-100 nm
2	Shape	Spherical	Spherical	Spherical, Lamellar
3	Stability	Thermodynamically Unstable, Weakly Kinetically Stable.	Thermodynamically Unstable, Kinetically Stable	Thermodynamically stable
4	Method of Preparation	High & Low Energy Method.	High & Low Energy Method.	Low Energy Method.
5	Polydispersity	Often High (>40%)	Typically, Low (<10-20 %)	Typically, Low (<10%)
6	Surface-to mass ratio (m2g -1)	0.07 – 70	70 – 330	130 – 1300

Nanoemulsion: - Emulsion is a system containing two immiscible phases and composed of at least three components: water phase, oil phase and surfactant phase. The nature of the surfactant determines the continuous phase (external phase) of the emulsion. (6) The thermodynamically stable transparent (translucent) dispersions of oil and water known as nanoemulsions, sub-micron emulsions (SMEs), mini-emulsions, and ultrafine emulsion are held together by an interfacial film of surfactant and co-surfactant molecules with a droplet size of less than 100 nm. The oil/water interfacial tension is extremely low in the dispersed phase, which typically consists of minute particles or droplets with a size range of 5 nm to 200 nm. Nanoemulsions are transparent because the droplet size is less than 25% of the wavelength of visible light. Nanoemulsion can occur quickly and occasionally spontaneously, usually without the use of high energy (7). Such nanoemulsions have been employed with a variety of surfactants with different properties (ionic or non-ionic). Among these, nonionic surfactants (such as sorbitan esters and polysorbates), anionic surfactants (such as potassium laurate and sodium lauryl sulphate), cationic surfactants (such as

quaternary ammonium halide), and zwitterions surfactants were the most commonly employed ones (quaternary ammonium halide)(4).

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

1) O/W Nanoemulsions where in oil droplets are dispersed in the continues aqueous phase
2) W/O Nanoemulsions where in water droplets are dispersed in the continuous oil phase
3) Bi-continuous (O/W/O, W/O/W) Nanoemulsions where in micro-domains of oil and water are inter-dispersed within the system.(6).

The O/W nanoemulsions further classified into three types based on the type of surfactants used which are as follows-

1) Neutral O/W nanoemulsions; neutral surfactant is employed in this type.
2) Cationic O/W nanoemulsion; cationic surfactants are employed in this case.
3) Anionic O/W nanoemulsion; the anionic surfactants are employed in this case.

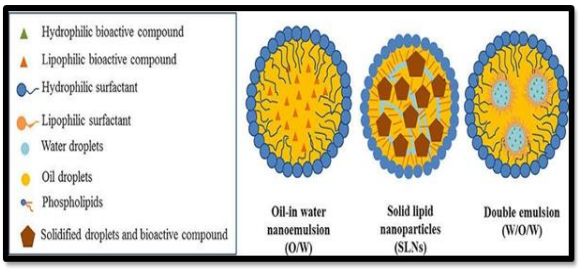


Fig No. 1- Water in Oil, Oil in Water and Bi-Continuous.

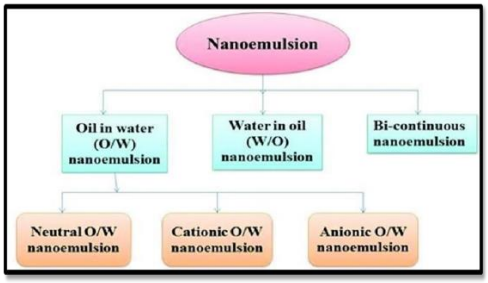


Fig. No. 2 – Type of Nanoemulsion.

Property: -

1) Size: - 20-500nm.
2) Shape: - Spherical.
3) Stability: - Thermodynamic unstable, kinetically stable.
4) Polydispersity: -Typically, low (<10-20%).
5) Transparency: - transparency makes nanoemulsions great materials for antibacterial finishing of white fabrics. (11)

ADVANTAGES: -

1) The use of nanoemulsions can increase the bioavailability of lipophilic medicines in the long run and their solubility in water.
2) Nanoemulsions improve the reproducibility of medication bioavailability and plasma concentration profiles..
3) Fine oil droplets enhance extensive distribution of the drug throughout the digestive system and help the stomach quickly empty, decreasing discomfort.
4) The use of Nanoemulsion as drug delivery systems can improve a drug's efficacy, allowing the total dose to be reduced and thus minimising side effects.
5) To deliver the product, various routes such as tropical, oral, and intravenous can be used.
6) The nanoemulsions may have great kinetic stability and optical transparency.
7) Nanoemulsions are thermodynamically stable systems, allowing for self-emulsification of a system whose properties are independent of the process used.(6)

8) Nanoemulsions have the potential to deliver peptides that are susceptible to enzymatic hydrolysis in the GI tract.(7)(6)(8).

DISADVANTAGES: -

1) The use of a high concentration of surfactant and co-surfactant is required for nanodroplets stabilization.
2) Low capacity for solubilizing high-melting substances.
3) To be used in pharmaceutical applications, the surfactant must be nontoxic.
4) Environmental factors such as temperature and pH affect the stability of nanoemulsions. When Nanoemulsion is administered to patients, these parameters change.(6)

Limitation: -

1) Manufacturing nanoemulsion formulation is an expensive process because reducing droplet size is difficult and requires specialized instruments and processes. For example, setting up a homogenizer (an instrument required for nanoemulsion formulation) is an expensive process. Again, micro-fludization and Ultrasonication (manufacturing processes) necessitate significant financial investment.
2) Nanoemulsion stability is quite poor, posing a significant problem during formulation storage for extended periods of time. Ostwald ripening is the primary cause of nanoemulsion formulation unacceptability. This is because small droplets with a high rate of curvature have greater solubility than large drops with a low radius of curvature.
3) Another factor that limits nanoemulsion manufacturing is the restricted in availability of surfactant and co-surfactant, which are required for the production of nanoemulsion. (9).

Characterization Of Nanoemulsion: -

1) Flocculation And Creaming: - Flocculation is the combining of globules to generate big clumps or floccules that rise or sink faster in the emulsion than individual globules. Creaming is the rising or settling of dispersed globules to form a concentrated layer. As a result, flocculation leads to creaming.
2) Cracking: - The separation of the dispersed phase as a layer is referred to as emulsion cracking. A creamed emulsion can be reconstituted by shaking or agitation, whereas a cracked emulsion cannot. Permanent instability is represented by cracking. Cracking of the emulsion may occur as a result of the following factors:

- addition of an emulgent of opposite nature,
- emulgent decomposition or precipitation,
- addition of a common solvent in which both the oily and aqueous phases are miscible,
- temperature extremes,
- microorganisms,
- Creaming.

3) Miscellaneous Instability: - Emulsions can degrade if they are stored at excessively high or low temperatures, or in the presence of light. As a result, emulsions are often packaged in airtight, coloured containers and maintained at room temperature.
4) Phase Inversion: - It is the conversion of an o/w emulsion to a w/o emulsion and vice versa. It is a physical procedure. Changing the phase volume ratio, adding electrolytes, and changing the temperature can all cause phase inversion. (22)

Review Of Literature: -

1) Patel RP, Joshi JR. An overview on nanoemulsion: a novel approach. International Journal of Pharmaceutical Sciences and Research. 2012 Dec 1;3(12):4640.

This review provides brief information about method of preparation and evaluation of nanoemulsion as drug carriers for improving the

delivery of therapeutic agents. 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, Transmission electron microscopy, thermal stability, release and in vitro skin permeation study.

2) Gurpreet, K. and Singh, S.K., 2018. Review of nanoemulsion formulation and characterization techniques. Indian Journal of Pharmaceutical Sciences, 80(5), pp.781-789.

Nanoemulsions are formulated using two different methods, the persuasion method and the Brute force method. Various characterization techniques for nanoemulsions include determination of entrapment efficiency, particle size as well as characterization through scanning transmission electron microscopy. Nanoemulsions are further evaluated by studying in stability and thermodynamic stability, shelf life, dispersibility, viscosity, pH.

3) Halnor, V.V., Pande, V.V., Borawake, D.D. and Nagare, H.S., 2018. Nanoemulsion: A novel platform for drug delivery system. J Mat Sci Nanotechol, 6(1), p.104.

One of the most efficient dispersed nanosystems is nanoemulsion having droplet size ranging to submicron size. Nanoemulsions are thermodynamically stable, clear, isotropic liquid mixtures of oil, water, surfactant and co-surfactant. The droplet size of nanoemulsion falls typically in the range 20-200 nm. The main difference between emulsion and nanoemulsion lies in the size and shape of particles dispersed in the continuous phase. This system is designed to address some of the problems associated with conventional drug delivery systems such as low bioavailability and noncompliance. Now a day nanoemulsions have attracted great attention in research, dosage form design and pharmacotherapy. The stability of nanoemulsion formulations can be maintained by a surfactant and co-surfactant. This review provides brief information about types, method of preparation, stability, evaluation and application of nanoemulsion.

4) Bhatt, P. and Madhav, S., 2011. A detailed review on nanoemulsion drug delivery system. International Journal of Pharmaceutical Sciences and Research, 2(10), p.2482.

Nanoemulsions are submicron sized emulsions that are under investigation as drug carriers for improving the delivery of therapeutic agents. These are the thermodynamically stable isotropic system in which two immiscible liquids are mixed to form a single phase by means of appropriate surfactant and cosurfactant. Nanoemulsion droplet sizes fall typically in the range of 20- 200nm and shows narrow size distribution.

5) Gupta, A., Eral, H.B., Hatton, T.A. and Doyle, P.S., 2016. Nanoemulsions: formation, properties and applications. Soft matter, 12(11), pp.2826-2841.

Nanoemulsions are kinetically stable liquid-in-liquid dispersions with droplet sizes on the order of 100 nm. Their small size leads to useful properties such as high surface area per unit volume, robust stability, optically transparent appearance. Additionally, they serve as model systems to understand nanoscale colloidal dispersions. High and low energy methods are used to prepare nanoemulsions, including high pressure homogenization, ultrasonication, phase inversion temperature and emulsion inversion point, as well as recently developed approaches such as bubble bursting method applications.

6) Debnath, S.U.B.H.A.S.H.I.S., Satayanarayana, K.V. and Kumar, G.V., 2011. Nanoemulsion-a method to improve the solubility of lipophilic drugs. Pharmanest, 2(2-3), pp.72-83.

The design of effective formulations for drugs has long beena major challenge, because drug efficacy can be severelylimited by instability or poor solubility in the vehicle. One of the most promising technologies is the nanoemulsion drugdelivery system, which is being applied to enhance the solu-bility and bioavailability of lipophilic drugs. Interest in Lipid Based Drug Delivery (LBDD) is relatively recent and relates to the developments in the past 10 to 15 years.

Aim & Objective

Aim: - A Review on Nanoemulsion Based System.

Objective: -

1) The main objective of nanoemulsion is particle size reduction for the better absorbtion of drug.
2) It increase the pharmacokinetic effect of the drug substance.
3) With the help of nanoemulsion the drug will release in controlled manner.
4) Nanoemulsion increases the safety profile of the drug.
5) It help to reduce the drug dosing and improve the bioavailability of drug.

Need For Developing Nanoemulsion: -

1) The major goals in designing nanoemulsion as a delivery system are to control particle size, surface properties and release of pharmacologically active agents so as to achieve the site specific action of the drug at the rationale rate and dose.
2) For instance, they help to increase the stability of drugs / proteins and possess useful controlled release properties.
3) The entropy of changes that favors dispersion is greater than the energy required to increase the surface of dispersion because the free energy of conventional emulsion is a direct function of the energy required to create a new surface between the oil and water phases and the addition of an emulsifying agent to reduce interfacial tension and thus stabilize the emulsion.

Plan Of Work: -

1) Literature survey.
2) Selection of Topic.
3) Search the research paper or review article of nanoemulsion on Google scholar.
4) Collect the article or research paper and Read out it.
5) Arrange a data in a proper manner.
6) Result and discussion.
7) Conclusion.

Actual Of Work

Component Of Nanoemulsion: -

Main three components of Nanoemulsions are as follows: (10)

1.Oil

2.Surfactant/Co-surfactant

3.Aqueous phase.

1)Oil: - The choice of a suitable oily phase is critical because it determines the choice of additional nanoemulsion ingredients, particularly in the case of O/W nanoemulsions. Typically, the oil with the greatest solubilizing potential for the selected drug candidate is chosen as an oily phase for the formulation of nanoemulsions. This contributes to the highest drug loading in the nanoemulsions. (8). After water, the oil phase is the second most significant vehicle due to its ability to solubilize lipophilic drug molecules and increase absorption through the body's lipid barrier. Because of its unique ability to penetrate cell walls, oil is extremely effective for lipophilic active medication delivery. (11)

Sr. No.	Oil Type	Example
1	Fatty acid esters	ethyl or methyl esters of lauric, myristic ,Oleic acid.
2	Saturated fatty acids.	Lauric, capric acid, myristic.

3	Unsaturated fatty acids.	linoleic acid. linolenic acid, Oleic acid

1) Surfactant: - The surfactant should promote microemulsification of the oily phase while simultaneously being capable of solubilizing hydrophobic medicinal molecules. The surfactant used in the nanoemulsion formulation is crucial. Surfactants with an HLB value of 10 are hydrophobic (such as sorbitan monoesters) and form w/o nanoemulsion, whereas surfactants with a high HLB (>10) are hydrophilic and create o/w nanoemulsion. Surfactants can be classified as follows. (11)

a) Non-ionic surfactant
b) Anionic surfactant
c) Cationic surfactant
d) Zwitter ionic surfactant

Table no. 3: Examples of Surfactant

Sr. No.	Types Of Surfactant	Example
1	Cationic surfactants	Amines and quaternary ammonium compounds such as Cetyl trimethyl ammonium bromide.
2	Anionic surfactants	They contain carboxylate groups. Soaps, sulfonates, divalent ions etc.
3	Nonionic surfactants	Fatty alcohols, glycerol esters, fatty acid esters etc.

2) Co-Surfactant: -A large amount of single-chain surfactants are required to reduce the interfacial tension between oil and water to the point where a nanoemulsion can form spontaneously. Because of the presence of fluidizing groups such as unsaturated bonds, co- surfactants increase the fluidity of the interface, which breaks the liquid crystalline or gel structure and alters the HLB value to spontaneously create nanoemulsions. (8) (11).

Table no. 4: Examples of Co-Surfactant.

Sr. No.	Types Of Co-Surfactants	Example
1	Short chain alcohols.	ethanol to butanol
2	Medium chain alcohols.	acids or amines
3	Short chain glycols	propylene glycol

3) **Aqueous Phase: -** The nature of the aqueous phase influences the droplet size and stability of nanoemulsion. As a result, when developing nanoemulsions, the pH and ionic concentration of the aqueous phase should be taken into account. pH values in the physiological milieu range from 1.2 (pH in stomach) to 7.4 and higher (pH of blood and intestine). Furthermore, the presence of different ions in the physiological milieu can have a significant impact on the characteristics of nanoemulsions (8) (11).

Table No. 5: List Of Oils Used In Nanoemulsions. (6)

Chemical Name	Name	Manufacture
Captex 8000	Glyceryl Tricaprylate (Tricaprylin)	Abitec

Witepso	90:10 % w/ w c12 Glyceride tri: diesters	Sasol pharmaceutical excipient
Captex 200	Dicaprate Glycol Propylene Dicaprylatel	Abitec
Isopropyl myristate	Myristic acid isopropyl ester	Fluka
Myritol 318	c8/c10 triglycerides	Russia
Captex 355	Caprate /Glyceryl Tricaorylate	Abitec

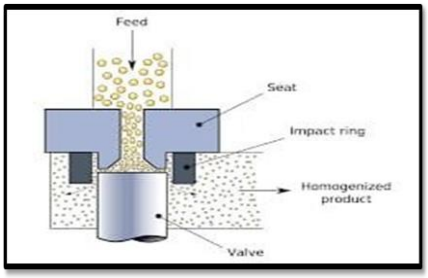
Techniques Of Preparation Of Nanoemulsion:

Nanoemulsions have very small particle sizes and are best manufactured with high- pressure equipment. The most frequent procedures for creating nanoemulsions are 'High pressure homogenization' which are employed both in the laboratory and on a large scale.

A) High Pressure Method: -

Nanoemulsions are frequently created using high energy technologies. High mechanical energy is utilized to create strong disruptive forces that break up big droplets into nano- sized droplets and produce high kinetic energy nanoemulsions. High energy technologies also give controls for emulsion stability, rheology, and colour. The following methods are associated with high energy methods: (14).

1) **High-Pressure Homogenenization:** High-pressure homogenizers provide high energy and uniform flow, resulting in the lowest particle sizes. As a result, high- pressure homogenizers are the most commonly employed to prepare nanoemulsions. High-pressure homogenizers are used to generate highly disruptive forces that result in nanoemulsions with exceedingly small particle sizes (up to 1 nm). The coarse emulsion is then fed under high pressure through a tiny aperture (500 to 5,000 psi). Several forces, including strong turbulence, hydraulic shear, and cavitation, are combined during this process to produce nanoemulsions with extremely small droplet sizes. (14) (15).



1) **Micro-Fluidization**: This method used a micro fluidizer, which is a device that uses a high pressure positive displacement pump (500-20 000 psi) to push the product out through the interaction chamber, which is made up of stainless steel micro channels on the impingement area, resulting in the formation of very small particles in the sub-micron range. The mixture is passed through the microfluidizer several times until the desired particle size is attained. The resulting product is also filtered to separate smaller droplets from bigger ones and to obtain a homogeneous nanoemulsion**.** (4)

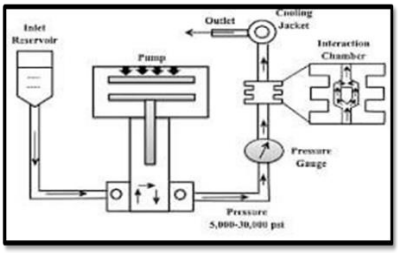


Fig. No.4: Micro-Fluidization (16)

Ultrasonication: The creation of Nanoemulsion is described in several research publications that aim to use ultrasonic sound frequency to reduce droplet size. At system pressures above the ambient value, another alternative is to employ a constant amplitude sonotrode. It is commonly understood that increasing the external pressure raises the cavitation threshold within an ultrasonic field, resulting in fewer bubbles. Increasing the external pressure, on the other hand, raises the collapse pressure of cavitation bubbles. This means that when cavitation occurs, the collapse of the bubbles becomes stronger and more violent than when the pressure is at atmospheric settings Because cavitation is the primary mechanism of power dissipation in a low frequency ultrasonic system**.** (4) (17).

Fig. No.5: Ultrasonication (16)

High-Shear Stirring Using a Rotor: - The mixing intensity of high shear stirring can reduce the internal phase droplet size, but preparing an emulsion with average droplet size less than 200 - 300nm is difficult. When a viscous phase, such as high viscosity oil, is introduced into the system, the efficacy of high shear stirring decreases, resulting in the creation of droplets in the micro range. Phase inversion is a low energy emulsification technology that produces a small droplet size range of less than 50nm (2) (18).

Fig. No.6: High-Shear Stirring Using a Rotor (16)

A) Low Energy Method: - For the manufacturing of nanoemulsion systems, these approaches need little energy. Low-energy emulsification technologies are more energy efficient since they use the systems' internal chemical energy and require only mild swirling to produce the nanoemulsion (15).

1) Phase Inversion Emulsification Method: - In this approach, the spontaneous curvature of the surfactant causes phase change during the emulsification process. Temperature, composition, and other parameters all influence the surfactant's spontaneous curvature. The two forms of phase inversion emulsification procedures are TPI methods, which involve PIT and PIC, and PIC methods.

a) Transitional Phase Inversion (TPI) **-**

i. Phase inversion temperature (PIT):- PIT is a low-energy emulsification technology that changes the optimal curvature of surfactants at constant composition by adjusting the temperature. The PIT method's emulsification efficiency was also found to be higher (1) than that of the PIC method (0.35). (20)

ii)Phase inversion composition (PIC):- At a fixed temperature, the PIC technique is based on a change in emulsion mixture phase (o/w to w/o or vice versa) produced by a change in emulsion mixture composition. Pouring the component (water or oil) over a mixture of the other two components (oil-surfactant or water-surfactant, respectively). Slow water addition, for example, transforms w/o micro-emulsions to o/w nanoemulsions (20).

b) Catastrophic Phase Inversion: -

i)Emulsion inversion phase (EIP): - The emulsion inversion point (EIP) method of emulsification is a low-energy and spontaneous emulsification technique. At constant temperature, it results in the intrinsic properties of thermodynamically stable microemulsions or liquid crystals being diverted to be nano-structured by progressive dilution with water or oil, respectively, to create thermodynamically unstable but kinetically stable direct or inverse nanoemulsions. A minor adjustment to the water or oil percentage (21)

2)Self-Nanoemulsion Method: - The self-emulsification approach produces nanoemulsions without affecting the surfactant's spontaneous curvature. Surfactant and/or co-solvent molecules diffuse rapidly from the dispersed phase to the continuous phase, causing turbulence and the formation of nano-sized emulsion droplets. The spontaneous emulsification method is another name for the self- emulsification process. (15).

3)Solvent Evaporation Technique: - In this procedure, a drug solution is created and emulsified into another liquid (a non-solvent for the drug), and then the solvent is evaporated, resulting in drug precipitation. A high-speed stirrer can be used to control crystal formation and particle aggregation. The solvent evaporation approach is quite similar to the hydrogel method. The main difference between this approach and solvent evaporation is that the drug solution is miscible with the drug antisolvent in this situation. (4) (20).

Evalution Test:-

1) **Viscosity Measurement: -** The viscosity of the nanoemulsions was measured in triplicate at 25°C using a Brookfield R/S plus rheometer (Brookfield Engineering, Middleboro, MA) with a C50-1 spindle**.** (26)
2) **Dye Solubilization**:- A water soluble dye is solubilized in the W/O globule's aqueous phase but dispersible in the O/W globule. An oil soluble dye is soluble in the O/W globule's oil phase yet dispersible in the W/O globule. (10)
3) **Dilutability Test**:- O/W Nanoemulsions are water dilutable, however W/O is not and undergoes phase inversion into O/W Nanoemulsions. (10).
4) **Fluorescence Test**: There are various oils that glow when exposed to UV light. When a W/O nanoemulsion is exposed to a fluorescence light under a microscope, the entire field fluoresces, whereas an O/W fluoresces in patches.
5) **Thermodynamic Stability Studies**: Following stress tests, the thermodynamic stability of drug-loaded Nanoemulsions was determined as follows:

a) **Heating Cooling Cycle**: Six cycles at temperatures ranging from 4°C to 45°C were performed on nanoemulsion compositions. The centrifugation test was then performed on the stable formulations.
b) **Centrifugation**: The nanoemulsion formulations were centrifuged at 3500 rpm and those that showed no phase separation were chosen for the freeze thaw stress test.
c) **Freeze Thaw Cycle**: Under conventional laboratory settings, the formulation was exposed to three freeze-thaw cycles between 21°C and +25°C. These experiments were carried out during a three-month period. (27) (10)

6) **pH Measurements**:- The pH was measured using a SevenMulti pH-meter outfitted with an InLab®Expert Pro electrode. The electrode was immersed in the resulting nanoemulsion to do the measurement. The provided data are the arithmetic mean of three measurements. The readings were taken at 25 degrees Celsius. (28)
7) **Dynamic Light-Scattering Measurements**:- Dynamic Light-Scattering measurements are done at 90° in a dynamic light scattering spectrophotometer equipped with a neon laser with a wavelength of 632 nm. The data is processed in the instrument's built-in computer. (25)
8) **Determination Of Encapsulation Efficiency:-** The encapsulation efficiency was determined and computed using the modified approach of Surassmo, Min, Bejrapha, and Cho (2010). The nanoemulsion was centrifuged at 1300 g and 5 C for 30 minutes after passing through Vivaspin concentrators of MWCO (Molecular Weight Cut Off) 100 kDa. The total phenolic content of the permeate was measured to calculate encapsulation efficiency. (29)
9) **Transmission Electron Microscopic Analysis:** Transmission electron microscopy (TEM) was used to examine the morphology of droplets. One A drop of diluted sample was deposited (100 times) on a 200-mesh sieve. film grid and allowed to dry

at ambient temperature The samples were let to dry for 10 minutes after being dyed with uranyl acetate prior to examination using an electron microscope. (31).

10) **Nanoemulsion Droplet Size Analysis:-**One of the major physicochemical properties of a nano-emulsion is droplet size distribution, which was determined using a diffusion method and a light-scattering particle size analyzer Coulter LS230. It measures particle size distribution using laser light diffusion. Polarization intensity differential scattering (PIDS) is an assembly that includes an incandescent light source, polarising filters, a PIDS sample cell, and seven photodiode detectors. It is used to measure the size distribution of droplets, such as when 0.5 ml of emulsion is injected into the measurement compartment (125 ml of water). The volume distribution is used to represent the results. (15)
11) **Drug Contain: -** This approach is used to calculate the amount of medication in the formulation. In this order, many approaches (particularly the Western Blot method) are used (14).

Application: - (32) (33) (34).

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 (or Injectable) administration of nanoemulsion is employed for a variety of purposes, namely nutrition eg. Fats, Carbohydrates, Vitamins etc.

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.

3)Pesticide Formulations Pesticide:- nanoemulsion formulations are formulations in which active chemicals used in treating or preventing the crops from any disease which affects agricultural yield have been incorporated into the nanoemulsion system. These types of pesticides have been categorized based on their target organisms.

4)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).

5)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 apolar media causes the denaturation of biocatalysts. The use of water-proof media is relatively advantageous.

RESULT AND DISSCUSION

Nanoemulsion drug delivery technologies efficiently overcome the low bioavailability disadvantage associated with hydrophobic medicines and other pharmaceutical or chemical components with high first pass metabolism. Researchers have employed high energy technologies to improve the delivery of medications and other pharmacological or chemical components. high energy methods are more expensive than low energy methods, which require less energy and are more efficient. Because high energy methods require low surfactant concentrations. . Furthermore, research papers show that a higher percentage of surfactant (much higher than CMC level) is used for the formation of Nanoemulsion, regardless of the route of administration, but there is a lack of toxicological evaluation of the prepared Nanoemulsion, which could be a broad research area in the future.

CONCLUSION

Nanoemulsion formulations have various advantages for pharmacological, biological, or diagnostic agent administration. For more than four decades, NEs have been used as whole parenteral feeding fluids in clinics. Although nanoemulsions are commonly used to provide aqueous insoluble medications, they have lately gained popularity as colloidal carriers for the targeted delivery of certain anticancer drugs,

photosensitizes, neutron capture therapy agents, or diagnostic agents. They can be easily targeted to the tumor location due to their submicron size.

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