IJPHT Journal
Papers Having Good Impact
International Journal of Pharmacy and Herbal Technology-ISSN NO: 2583-8962 (Online)

A SYSTEMATIC REVIEW ON NANOEMULSION

Jiwan P.Lavande, Sanjay.K.Bais,Shamal Lokhande
Fabtech College of Pharmacy, Sangola -413307 India
Email Id of Corresponding Author- shamaldlokhande@gmail.com

ABSTRACT :

This review examines and summarizes the creation, characteristics, attributes, and uses of nano-emulsions.Submicron-sized emulsions known as nanoemulsions.Using the right surfactant, two non-reactive liquids (oil and water) come together to form a phase in a thermodynamically stable isotropic process called nanoemulsion. Due to their small size, nanoemulsion is stable against emulsification or precipitation; The main mechanism of nanoemulsion decomposition is Ostwald ripening.The diameter and surface area of nanoemulsion droplet are have a significant impact on the biological behavior of formulation. Future development in drug therapy, cosmetic, diagnostic, and biotechnologie all seem very promising when it comes to nanoemulsion. The purpose of this review is to discuss the advantage and disadvantage of nanoemulsion, including different preparation method, characterization methods, and application of submicron emulsions in various fields such as pharmaceutical cosmetics, chemotherapy, and other administration methods.

Keywords *– Nanoemulsion, Ostwald ripening , pharmaceutical cosmetics*

INTRODUCTION :

Technological advancements on the nanoscale, or typically between 0.1 and 100 nm,are referred to as nanotechnology.The use of nanotechnology in medicine and pharmacy has increased in the last few years."NANOPHARMACEUTICALS" are the name given to medications created using nanotechnology.Various surfactants with different properties (ionic or non-ionic) are used in such nanoemulsions. Ntawm's law applies to non-ionic surfactants (polysorbates, sorbitan ester), thiab anionic surfactant potassium laurate and sodium lauryl sulfate, zwitterion quaternary ammonium halide, cationic surfactant quaternary ammonium halide.A kind of dispersed particles called nanoemulsions is employed in pharmaceutical and biological aids and vehicles, and it has enormous possibilities for future of cosmetics, medication therapy, diagnostic, and biotechnology.Size between 50 and 1000 nanometers. Typically, the average size of a droplet is between the 100 to 500 nm.correspondingly Sub-micron emulsion (SME) is referred to as and mini-emulsion are synonymous terms.

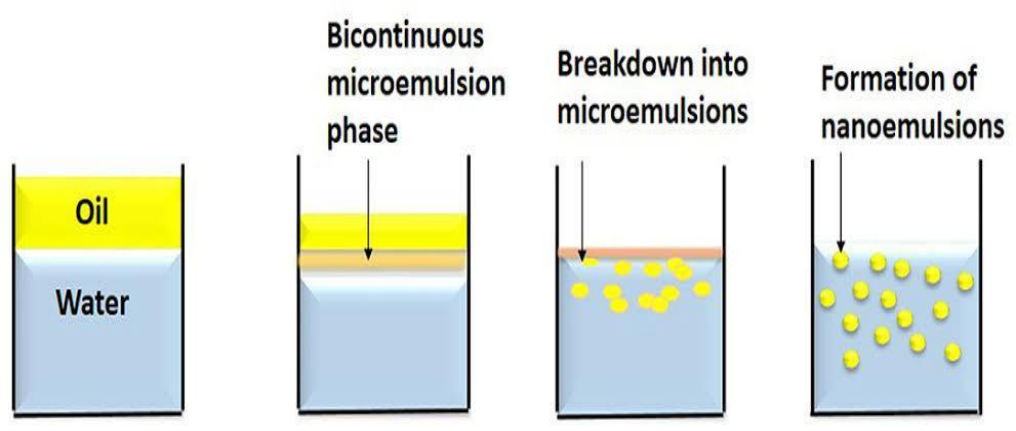

Fig.no 1 Nanoemulsion

Early nanoemulsions had average droplet sizes and were in the O/W type. diameter is range between the 50–1000 nm. More recently, nanoemulsions have been divided into three groups, including Three types of dispersions are known: O/W oil in aqueous phase ; water-in-oil W/O ; water in oil, phase and bicontinuous interdispersed water and oil microdomains within the system.where a system has both W/O and O/W emulsions are at same time. Both lipophobic and hydrophobic surfactants are utilized simultaneously are stabilize these two emulsions.

Table no. 1 Properties of emulsions

Emulsions	**Droplet size**	**Thermodynamic stability**	**Apperance**
Macroemulsions	0.1-100 um	Unstable	Turbid
Microemulsions	5-100 um	Stable	Transparent
Nanoemulsions	5-200 um	Unstable	Transparent

Because of their extremely narrow range of particle sizes, nanoemulsions are best made with high-pressure machinery. The two most popular techniques for creating nanoemulsions, both in the lab and in industry, is the "high-pressure homogenization and microfluidization process".For the preparation of nanoemulsion, other techniques such as the in-situ emulsifications and ultrasonification are also appropriate.Techniques of the Preparation of the Nanoemulsion[1,3,4]

Components of Nanoemulsions[5]

1) Oil part
2) Surfactant part
3) Cosurfactant part
4) Aqueous phase part

Technique used in preparation of Nanoemulsions

1) High pressure homogenization technique
2) Ultrasonication technique
3) Phase inversion technique
4) Spontaneous emulsification technique
5) Solvent evaporation method
6) Hydrogel technique

1.High pressure homogenization machine:-

Preparation of nanoemulsions requires high-pressure homogenization. This homogenizer uses a high-power homogenizer and a piston homogenizer to produce nanoemulsions with small particles up to 1 nm.The process of dispersing two liquid (oil & water) requires high pressure 500-5k psi to mix through a small inlet hole.. This expose product to pressure and hydraulic shear, resulting in a perfect emulsion product.The resulting phospholipid monolayer separates the liquid lipophilic core from the surrounding aqueous phase. The only drawback of this method is its high efficiency, which is the high consumption and work due to the increase in the emulsion temperature.energyconsumption [6,7,8]

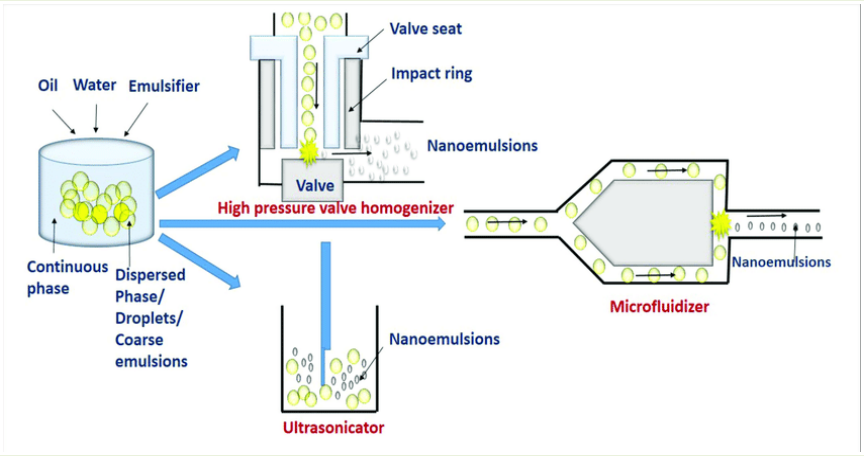

Fig. no 2 Process High pressure homogenizer

Advantages:

- applied to thermolabile materials with efficacy.
- The Scale-up simplicity and minimal in batch-to-batch variations
- restricted drug nanoparticulate size distributions.
- adaptability in managing of the medication's quality

2. Ultrasonication

Numerous research papers that aim to reduce the droplet size by using the ultrasonic sound frequency report on preparation of nanoemulsions. When the system pressure is higher than the ambient pressure, another option is to employ a constant amplitude ultrasonic generator. External pressure is known to increase the onset of cavitation of the ultrasonic field, thus

preventing further bubbles from coming out of the way. However, increasing the external pressure may cause the cavitation bubble to collapse.

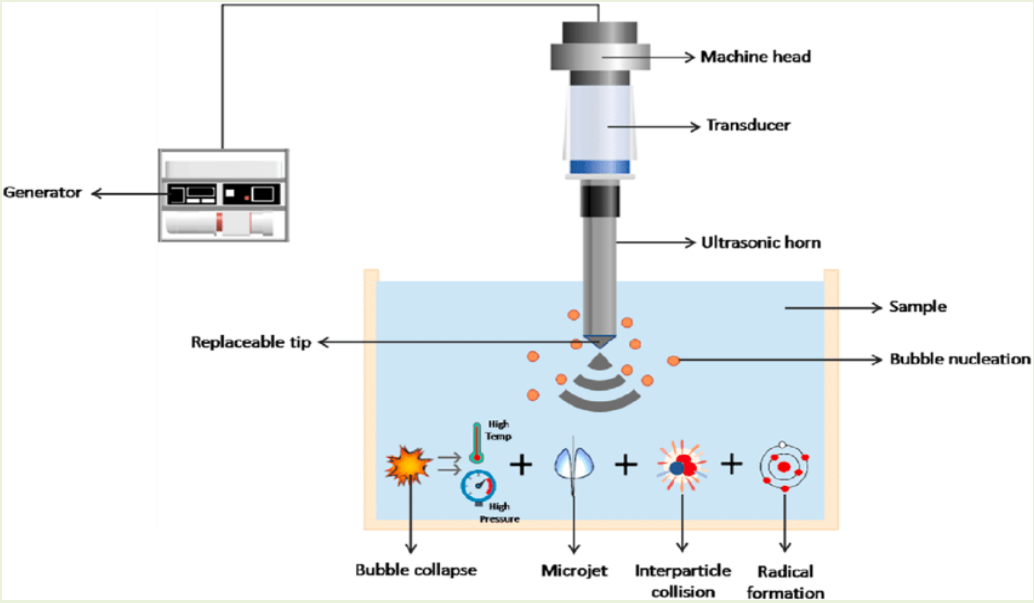

Fig.no 3 Process of ultrasonication

pressure. This indicates that when cavitation occurs, bubble collapse will be stronger and greater than atmospheric pressure.Changes in navigation usage may result from cavitation, which is the main mechanism of power dissipation in low-frequency ultrasound systems.[6,7,8]

3. Phase inversion method:-

Using this technique, phase transitions brought about by the emulsification pathway produce chemical energy that leads to fine dispersion. Phase variations are caused by altering the emulsion's composition while regulating the temperature, and vice versa. At that time, Shinoda and co. did the first investigation on the phase inversion temperature, and they found that because the polymer chain breaks .[6,7,8]

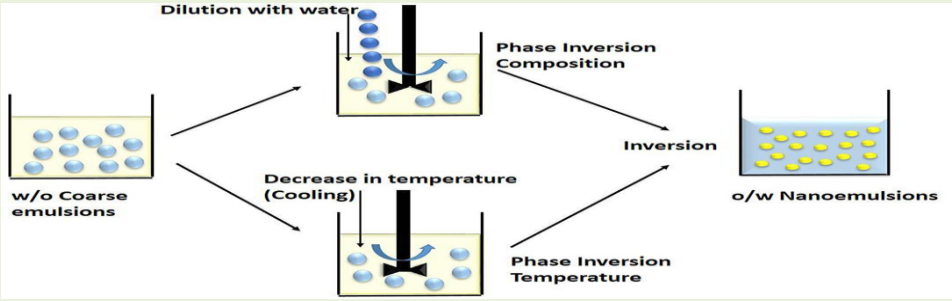

Fig. no 4 Process of phase inversion method

4. Spontaneous emulsification technique :-

- It consist of the main three ssteps.

  1.Use oils, hydrophilic surfactants, water-miscible solvents, and lipophilic surfactants to create homogeneous organic solutions..

  2.Add the organic and aqueous phases to the magnetic stirrer to form an oil-water eemulsion.

  3Afterwardss, water-miscible particulates are eliminated using low-pressure evaporation. [6,7,8]

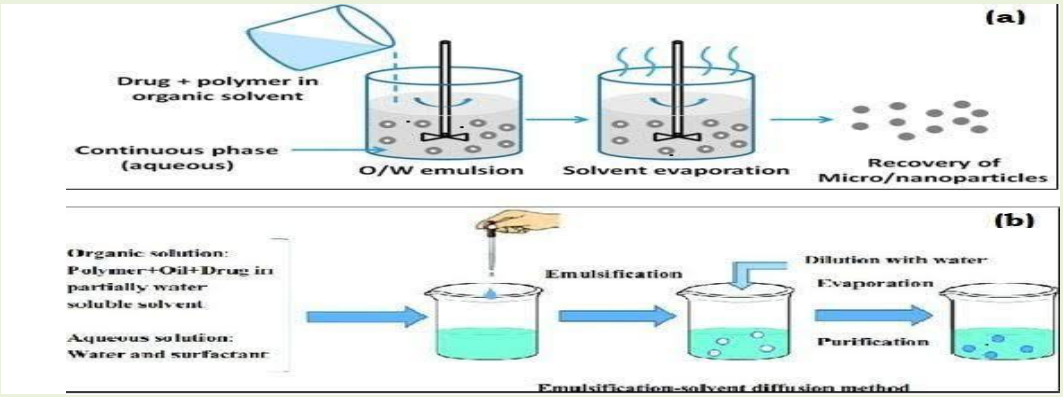

Fig. no 5 Process of spontaneous emulsifivation

5. Solvent evaporation method:-

This method requires preparing the drug solution and then emulsifying it in a different liquid that is not heavy drug. Precipitation of drug results from solvent evaporation. High shear forces can be produced to control particle aggregation or crystal formation with the help of the high-speed stirrer.[6,7,8]

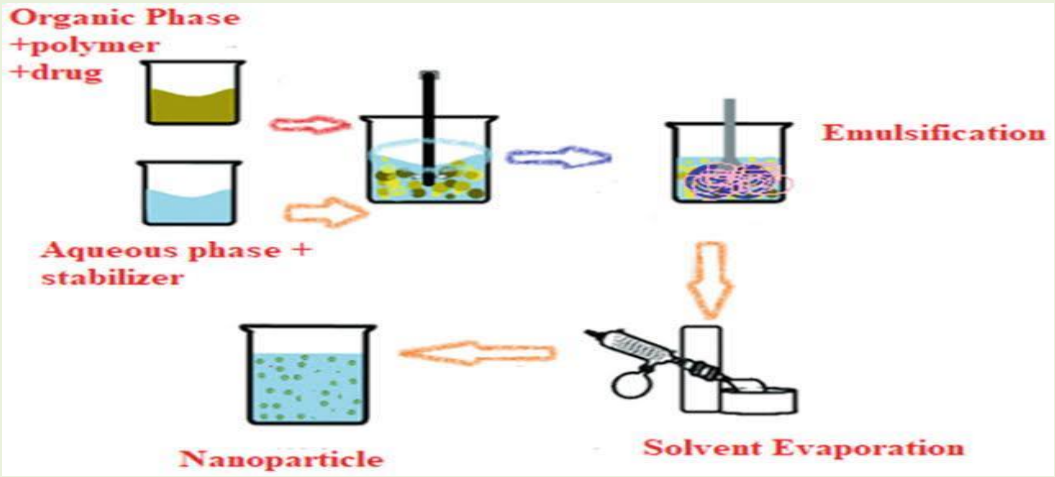

Fig. no 6 Process of solvent evaporation technique

6. Hydrogel technique:-

It can be compared to the process of evaporation of the solvent. Miscibility of the solvent with the antisolvent is the only difference between the two technologies. Ostwald ripening and crystal growth are inhibited by higher shear force.[6,7,8]

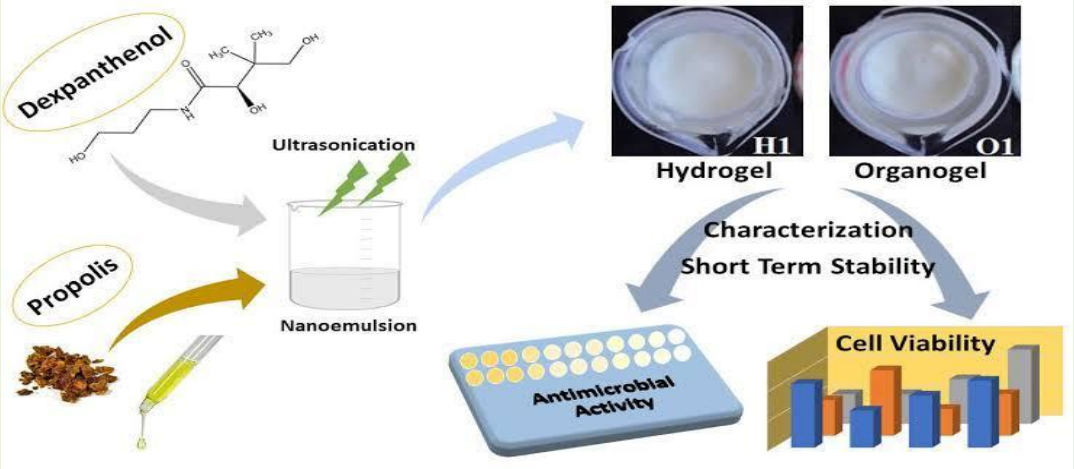

Fig . no 7 Process of hydrogel method

CHARACTERIZATION OF NANOEMULSION

Determination of encapsulation efficacy

To ascertain the amount of drug imbedded in the formulation, the heavy formulation is dissolved in an organic ultrasonic solvent, and the drug is then extracted into a buffer.After appropriate dilution, the content of the drug is determined by spectrophotometric analysis of the λmax extract of the drug. against an appropriate blank. It is possible to compute the drug's loading efficiency (LE) and entrapment efficiency.Drug LE is the drug content in the product consumed (mg) / total product weight (mg) × 100, and drug EE is the drug content in the product taken (mg) / total additional product (mg) × 100. MedicineHigh-performance liquid chromatography in reverse phase could also be used to determine content (HPLC) methods. Using this method, Singh et al. discovered the primaquine concentration and reported a 95% encapsulation formulation efefficiency[2]

- **Parenteral delivery of (O/W) and (W/O) nanoemulsions is appropriate.**

The Malvern Zetasizer is able to use photon correlation spectroscopy (PCS) to determine the size and PDI of nanoemulsions by monitoring changes in light scattering due to the Brownian motion of particles over time.The fundamental tenet of PCS is that, relative to larger-sized particles, smaller particles move faster.particles. Submicron particle diffraction of the laser beam is present in the solution. Particle diffusion causes the laser beam intensity to change suddenly around the average value of the angle, which varies depending on the particle size. The photoelectron time calculated line width distribution histogram produced by correlation function can be used in to determine the size of fragment. Weighing a portion of the particle to determine its size .Use double distilled water to dilute the formula to create a uniform dispersion. The resulting solution should be used right away to measure PDI and particle size. PDI has two values: zero for monodisperse systems and burst 1 for polydisperse particles Đorđević et al. used this to assess the PDI and particle size of the risperidone nanoemulsion. The average particle

size distribution is less than 0.15, and the average particle size is approximately 160 nm. Using the same technique, Singh et al. also observed that primaquine nanoemulsions had particle sizes ranging from 20 to 200 nm.[2]

Development and characterization of osmotic tablet.

The primary objective of this review was to make and test permeable osmotic tablets that can expand with controlled porosity for the treatment of herpes simplex. This formulation strives to improve bioavailability, reduce useful organ recurrence, eliminate unwanted design drugs, and improve patient consistency. Acyclovir is a manufactured simple of a purine nucleoside that is especially initiated by thymidine kinase, which is delivered by the Herpes Simplex Infection (HSV). It hinders viral DNA polymerases and fills in as a chain eliminator. Direct pressure was the strategy used to make the tablets, which were then profound covered to make a sum of nine formulations (F1-F9). The produced granules' flow and compression properties were assessed before compression. Also considered for the in vitro drug release investigation was a prepared osmotic drug delivery device. During pill disintegration, the coating did not exhibit any signs of leaking and remained stable. The range of the coated tablet's weight increase percentage was determined to be 1.98–2.40%. Semipermeable membrane has a 240 m thickness and can tolerate pressure during disintegration. [17]

Advantages

- Boost the absorption rate. removes fluctuations in absorption. aids in the solubilization of lipophilic medication. gives medications that are water-insoluble an aqueous dosage form. boosts the bioavailability. The product can be administered via oral, intravenous, and tropical routes.
- Drug moiety penetration that is quick and effective. beneficial for masking tastes. Patient compliance is increased by liquid dosage forms. smaller amount of energy needed.
- Thermodynamic stability in nanoemulsions enables the system to self-emulsify, resulting in properties that are independent of the procedure used. The same nanoemulsions can transport hydrophilic and lipophilic medications.
- The effectiveness of a medication can be increased by using nanoemulsion delivery systems, which minimizes side effects by enabling a reduction in the overall dosage.[9]

Disadvantages

- Temperature and pH levels are two examples of environmental factors that affect nanoemulsion stability. When patients receive nanoemulsion, these parameters shift. Preparation of nanoemulsions requires high-pressure homogenizers, ultrasound, microfluidic beds, and other technologies. Only recently has such equipment (like the Microfluidiser) become accessible. To stabilize the nanodroplet, high quantitie of surfactant and cosurfactant are required. Melting ability is limited at high melting points. When using surfactant in medicine, it should be non-toxic.

- Especially in the cosmetic industry, production costs are high due to the use of expensive materials and high emulsifiers.Understanding the function of cosurfactants and surfactants as well as the process that produces submicron droplets is challenging.
- The advantages of classical macroemulsion systems outweigh those of nanoemulsion. The chemistry at the interface play a crucial role in the creation of nanoemulsion. However, it's unclear how the interfacial chemistry works. Due to their limited solubility, difficult for substances with a high melting point.[9]

APPLICATIONs OF NANOEMULSION

1.Nanoemulsion used as mucosal vaccine

More protein or dormant bacteria can be delivered to mucosal cells by nanoemulsion, which helps eliminate antibodie. Initial use of anti-HIV and anti-influenza drugs may lead to clinical trials. Application of the protein to the mucosa appears to be an adjuvant and is supported by the immune system. To finish proof of concept animal testing for other vaccinations, like those against hepatitis B and anthrax, more research is being conducted. Intraperitoneal vaccination of guinea pig, pig and mouse with recombinant HIV gp120 antigen mixture. Anti-virus gp120 was detected by IgG with mouse anti-emulsion. -gp120 IgA, genital and bronchial antibodies[10,11]

2. Non-Toxic Disinfectant Cleaner: Nanoemulsion

A non-toxic dishwasher for the travel, healthcare, hospitality, food processing and military industries from EnviroSystems, Inc. It has developed applications that eliminate many diseases, especially tuberculosis, bacteria and harmless diseases, within five to ten minutes. from different groups of killers. The Product does not require labels with warnings. It doesn't aggravate It can be breathed, absorbed through the skin, or ingested without causing any harm. The antiseptic composition consists of oil droplet nanospheres. to form a NE, #106 mm that are suspended in water needing minuscule quantities of the active PCMX (parachlorometaxylenol) is the component.[15]

3.Technology of Cell Culture Utilizing Nanoemulsion

Two applications of cell culture include the synthesis of proteins, in vitro testing, and the creation of biological materials like antibodies. Different substances can be added to the culture medium and combined with specific chemicals or blood to encourage cell multiplication.The benefits of applying nanoemulsions to the technology of cell culture are improved absorption in cell cultures of nutrients soluble in oil;enhance the viability and development of cultured cells, and Permission to conduct oil-soluble drug toxicity investigations in cell cultures[12]

4.Nanoemulsionsin used in Cancer Therapy

Nanoemulsions can be employed as carriers for long-term drug release following intratumoral and intramuscular injection [W/O systems] when employing cancer medications.Additionally, it improves transdermal drug delivery because it facilitates the transportation of anti-cancer medicationsvia the skin's lymphatic penetration and Its system is also non-irritating.[14,15]

5.Utilizing nanoemulsion in targeted drug delivery systems and cancer therapy

Impact of the formulation and particle composition of the gadolinium (Gd) lipid nanoemulsion (Gd-nanoLE) on the biodistribution of D1-179, Gd, following intravenous (IV) administration in melanoma-treated hamsters using neutron capture**.**Applications for Cancer. The results of biodistribution showed that HCO-60 and Brij 700 extended the time that Gd remained in the blood and increased the way it accumulated in tumors. After transdermal administration, the drug usually forms in the outer layers of the skin and there is little escape.As a result, the overall bioavailability was 70.62%. The oral PCL medication's bioavailability is increased by D-tocopherol, polyethylene glycol 1000, and P-glycoprotein Labrasol, which all prevent the efflux of succinate.This work offers distinctive proof that lipophilic high molecular weight PCL medications are located in the dermis. **[13]**

7. Transdermal

Rats with paw edema caused by carragenan were given an optimized nanoemulsion formulation and its anti-inflammatory effects were compared to marketed gel. Significant inhibition was found for the developed nanoemulsion, indicating enormous potential. for indomethacin transdermal application utilizing nanoemulsions to apply transdermally. Following a 24-hour administration, it show anti-inflammatory effect and percent inhibition value were discovered to be high 81.2% for the formulation of nanoemulsions as in contrast to naïoemulsion gel 64.5%or celecoxib gel 43.7%. Aceclofenac nanoemulsion shown enhanced anti-inflammatory capabilities 82.2% in both in vitro and in vivo investigations when compared to traditional gel and nanoemulsion gel formulation 71.4%.[14]

8.The use of nanoemulsion in medication delivery to the lungs

Since it enables more medications to be delivered from aerosols to the site of action for first-pass metabolism and disease treatment, the lung is a crucial target for drug delivery. The medication is in the distribution area and the medication is absorbed into the body. In the process of enhancing alveolar drug solubility through their water solubility, colloidal carrier or nanocarrier systems offer various benefits for the delivery of pulmonary medications, including the potential to generate a drug combination that lengthens the duration of drug release. Internalization by cells lowers the frequency of dosages, improves patient compliance, and lessens the likelihood of adverse effects.[14]

9.In a gene delivery vector, nanoemulsion

Genetically modified liposomes have been replaced by emulsion systems. Other studies of emulsions used for non-pulmonary gene delivery have shown that emulsion/DNA complexes bind more strongly than liposomal carriers.. Liposomes were not as effective in delivering this continuous gene delivery as the emulsion approach. Silva et al. In the first amine-based drug, the stearylamine component was evaluated, which are cationic lipids that can interact electrostatically in cationic nanoemulsions and affect DNA compaction in cationic lipid nanoemulsions. . They are put to the test because they have a good effect on the oil/water connection.The impact of time and the stearylaminomine incorporation phase (oil or water) of complexity and various incubation temperatures were investigated.The description was dynamic light scattering (DLS) was used. [16]

10. Parentral dilivery

Because intravenous administration is so strict, nanoemulsion has advantages in this route of administration, especially with regard to the requirement for a smaller droplet size in the formulation greater than one micrometer. Nanoemulsions contain nutrients - fats, carbohydrates, vitamins, etc. It can be used for various purposes in the delivery of parenteral or parenteral drugs, for example, when nanoemulsion formulations are used, it has the advantages of macroemulsion systems. When taken parenterally, nanoemulsions are eliminated more slowly than macroemulsions and therefore remain in the body longer.Parenteral delivery of O/W and W/O nanoemulsions is appropriate.[14]

11.Fast dissolving films

Some patients have difficulties in swallowing or chewing solid dosage which forms risk or fear of chocking so this is a major problem in the use of tablets. Oral dissolving film is a new drug delivery system for oral delivery of drug. The oral route of drug administration is the most important method of administration of drug for systemic effect, despite of tremendous advancement in drug delivery system. Its ease of administration, pain avoidance and various advantages over other routes is the reason that the oral route achieved such popularity.[18]

Summary table

Table no 2: Difference Between the emulsions, nanoemulsions,microemulsions

Emulsions	Nanoemulsions	Microemulsions
They have outstanding kinetic stability	Inherently unstable	They are have some degree of kinetic stabilites.
They are thermodynamically unstable;phase separation will eventually occur	It is thermodynamically stable and has no phase change.	stable thermodynamics
Emulsions seem hazy.	Nanoemulsion are clear and	It is clear microemulsion

	translucent	
The processes used to prepare the emulsion demand a significant energy input.	Preparation techniques don't need energy to operate.	Preparation techniques don't need energy

Table no 3: List of oils

Name	Chemical name
Captex355	Glyceryl Tricaorylate,Caprate
Captex200	Propylene Dicaprylate,Dicaprate Glycol
Captex8000	Glyceryl Tricaprylate (Tricaprylin)
Witepsol	90:10 % w/w c12 Glyceride tri: diesters
Myritol318	C8 and C10 triglycerides
Isopropyl myristate	Myristic acid isopropyl ester

Table no 4. List of surfactant

Name	Chemical name
Tween 20	polyoxyethylene Sorbitan Monolaurate
Tween80	polyoxyethylene [20] sorbitanmonooleate
Labrasol	caprylocaproyl macrogol 8 glycerides
Labrafil M 1944	oleoyl macrogol-6 glycerides
Cremophore RH-40	polyoxly 40-hydrogenated castor oil
PlurolOleique CC	Polyglyceryl 3 oleate

Table no 5. List of co surfactant

Name	Chemical Name

transcutol-P cosurfactant	diethylene glycol monoethyl ether
ethylene glycol cosurfactant	Ethane 1;2 diol
propylene glycol cosurfactant	1;2 propanediol

CONCLUSION

Formulations in the form of nanoemulsions have various benefits for the delivery of pharmaceutical, biological, or diagnostic agent. For over forty years, total parenteral nutrition fluids have been made using nanoemulsions in clinics. Nanoemulsions are primarily used as delivery systems for aqueous insoluble pharmaceuticals, but in recent times, they have drawn more interest as the colloidal carrier for the targeted to delivery of different anticancers medications, photo sensitizer, agents for neutron capture therapy, or diagnostics. They are easily targeted to tumor site due to the their submicron size. In the near future, more research and development work is anticipated to be done in order to clinically realize these targeted delivery vehicles. NE formulations have various benefits when it comes to the administration of medications, biologicals, or diagnostic agents. For over forty years, NEs have been utilized in clinics as total parenteral nutritional drinks. Numerous additional drug delivery products Additionally, products like Diprivan®, Liple®, and Ropion® have arrived at the retail outlet. Even though NEs are primarily perceived as vehicles When it comes to giving out water-insoluble medications, they have more lately attracted more focus as the colloidal carriers for the targeted administration of different anticancer medications, photosensitizer, agents used in neutrons capture therapy and diagnostics

REFERENCE

1) Current Update on Nanoemulsion: A Review Himesh Soni Sarvesh Sharma11D.H.S. Bhopal Madhya Pradesh, 6.
2) INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACY AND CHEMISTRY by Pranita Savardekar and Amrita Bajaj.Department of Pharmaceutics, SVKM‟s Dr. BhanubenNanavati College of Pharmacy ,312
3) Nanoemulsion: A Pharmaceutical Review by Shah P, Bhalodia D1Shelat P1 Department of Pharmaceutics, Saraswati Institute of Pharmaceutical Sciences,Dhanap, 1K.B.Institute of Pharmaceutical Education and Research January-June 2010 , 1 (1),1
4) 4. A Herbert. M Rieger, G S Banker, Pharmaceutical Dosage Forms: Disperse systems;Marcel Dekker Inc, 3(8),339,340,343,344
5) .Anton, N., Benoit, J.P., and Saulnier, P. Design and production of nanoparticles formulated from nano-emulsion templates-A review, Journal of Controlled Release,2008, 128, 185
6) Jumaa M, Mueller BW. Formulation and stability of benzodiazepines in a new lipid emulsion formulation. Pharmazie 2002;57:740-3.

7) Shaji J, Joshi V. Self-microemulsifying drug delivery system (SMEDDS) for improving the bioavailability of hydrophobic drugs and its potential to give sustained release dosage forms. Indian J Pharm Educ 2005;39:130-5.
8) Carey MC, Small DM, Bliss CM. Lipid digestion and absorption. Ann Rev Physiol 1983;45:651-77.
9) Date AA, Nagarsenker S. Parenteral microemulsion: an overview. Int J Pharm 2008;355:19-30.
10) 16. Makidon, P. E., Bielinska, A. U., Nigavekar, S. S., Janczak, K. W., Knowlton, J., Scott, A. J., ... & Baker Jr, J. R. Pre-clinical evaluation of a novel nanoemulsion-based hepatitis B mucosal vaccine. PloS one,2008, 3(8), 2954.
11) 17. Arbor, A. Nanoemulsion vaccines show increasing promise Oil-based nasal vaccine technique produces immunity against smallpox, HIV. AIDS Res Hum Retroviruses, 2008,24, 1-9.
12) 21. Ichikawa, H., Watanabe, T., Tokumitsu, H., & Fukumori, Y.Formulation considerations of gadolinium lipid nanoemulsion for intravenous delivery to tumors in neutron-capture therapy. Current drug delivery, 2007,4(2), 131-140.
13) Khandavilli, S., & Panchagnula, R. (2007). Nanoemulsions as versatile formulations for paclitaxel delivery: peroral and dermal delivery studies in rats. Journal of Investigative Dermatology, 127(1), 154-162
14) Tamilvanan S. Submicron emulsions as a carrier for topical (ocular and percutaneous)and nasal drug delivery.Indian J. Pharm. Educ. 2004,38(2):73-8.
15) Heidi MM, Yun-Seok R, Xiao W. Nanomedicine in pulmonary delivery. Int. J.Nanomed. 2009; 4: 299–319.
16) Junyaprasert B.V, Muller H.R, Souto B.E et al.: Q10 loaded NLC versus nanoemulsions; stability, rheology and in vitro skin permeation. Int. J Pharm. 2009; 377:207-214.
17) Brahmbhatt, H., Lavande, J. P., Patil, V. V., Sheikh, I. A., Rohit, C. S. A. K., Hussain, K., & Ranjan, R. (2023). Formulation, Development and Characterization of Osmotic Tablets Containing Acyclovir. Rivista Italiana di Filosofia Analitica Junior, 14(2), 1647-1655.
18) JP Lavande, A.A Agnihotri, R.N Ade, P.B Itekar, P.A Pangarkar, AV Chandewar
Indo American Journal of Pharmaceutical Research 3 (7), 1575-1593, 2013