A Review on Nano-Emulsion

Rohit Chavan[1], Pragati Chavan[2], Amol Ban[3], Dr.Samrat A. Khedkar[4]
[1,2,4]*Students of JBVP's Vidya Niketan College of Pharmacy Lakhewadi, Pune*
[3]*Associate Professor, Department of Pharmaceutics, JBVP's Vidya Niketan College of Pharmacy, Lakhewadi, Pune.*

***Abstract*—Nanoemulsions are nanoscale colloidal dispersions composed of oil, water, and surfactants, characterized by droplet sizes typically ranging from 20 to 200 nm. Owing to their high kinetic stability, transparent appearance, and enhanced solubilization capacity, nanoemulsions have gained significant attention across pharmaceutical, cosmetic, food, and industrial applications. This review provides a comprehensive overview of nanoemulsion systems, beginning with their fundamental principles and progressing to their advantages, such as improved bioavailability, controlled drug release, and enhanced stability of encapsulated compounds. Potential limitations, including formulation complexity, high surfactant requirements, and physical instability under extreme conditions, are also discussed. Different types of nanoemulsions oil-in-water, water-in-oil, and bicontinuous systems along with their key components, such as oils, surfactants, co-surfactants, and aqueous phases, are described in detail. Various preparation methods, including high-energy (ultrasonication, high-pressure homogenization) and low-energy techniques (phase inversion, spontaneous emulsification), are examined with emphasis on their mechanism and applicability. Evaluation parameters such as droplet size analysis, zeta potential, viscosity, pH, stability testing, and morphology assessment are reviewed to highlight their importance in characterizing formulation performance. Finally, the wide-ranging applications of nanoemulsions from drug delivery and wound healing to food fortification and agrochemical enhancement are summarized, underscoring their growing relevance in modern technological advancements.**

***Index Terms*—Nano-emulsion, types, application, Methods.**

I. INTRODUCTION

Nanoemulsions, often referred to as submicron emulsions, ultrafine emulsions, and namoemulsions, are colloidal particulate systems characterized by their submicron size. These systems are recognized as thermodynamically and kinetically stable isotropic dispersions, comprising two immiscible liquids, such as water and oil. They are stabilized by an interfacial film formed by an appropriate surfactant and co-surfactant, resulting in a single phase. Numerous surfactants, both ionic and non-ionic, have been employed with these nanoemulsions. [1]

forming the primary mechanism of the disintegration of nanoemulsions. The primary use of nanoemulsions is in the production of nanoparticles by employing a polymerizable monomer as the dispersing phase (a process known as "nanoemulsion polymerization"), in which nanoemulsion droplets serve as nanoreactors. The use of nanoemulsions as formulations, specifically for targeted and controlled drug administration, is another intriguing use that is undergoing active development. The creation of nanoparticles utilizing a polymerizable monomer as the disperse phase, where nanoemulsion droplets function as nanoreactors, is the primary use of nanoemulsions. [3]

II. ADVANTAGES OF NANOEMULSION

- Nanoemulsions are an efficient transport method because of their increased surface area and free energy.
- hey do not show the problems of inherent creaming, flocculation, coalescence and sedimentation.
- It can be formulated in variety of formulations such as foams, creams, liquids and sprays.
- They are non-toxic; non-irritant hence can be easily applied to skin and mucous membranes.
- It can be administered orally if the formulation contains surfactants which are biocompatible

III. DISADVANTAGES OF NANOEMULSION

- Large concentration of surfactants /cosurfactants is required for stabilization.
- Its stability is affected by temperature and pH.
- Instability can be caused due to Oswald ripening effect. [2]

IV. COMPONENTS OF NANO EMULSION

Main three components of Nanoemulsions are as follows:

a) Oil
b) Surfactant/Co-surfactant
c) Aqueous phase

Colloidal dispersions made up of an oil phase, aqueous phase, surfactant, and cosurfactant in the right proportions are called nanoemulsions. Low interfacial tension is the foundation of nanoemulsions, in contrast to coarse emulsions that are micronized by external energy. This is are a number of ways that nanoemulsions can theoretically be utilized to deliver medications to patients, topical use of nanoemulsions has drawn more attention. [4]

Table:1. The Formulation Components of a Nanoemulsion Are Described

Sr. No.	Components	Examples
01	Oil	Castor oil, Corn oil, Coconut oil, linseed oil, Mineral oil, olive oil, groundnut oil
02	Surfactant	Polysorbate20, Polysorbate80, Polyoxy 60, DGME, Sorbitan monooleate, Caprylic glyceride
03	Co-surfactant	Ethanol, glycerine, PEG300, PEG400, Polyene glycol, Poloxamer
04	pH Stabilizer	Sodium hydroxide or hydrogen chloride, Triethanolamine
05	Preservatives	Methyl Paraben, Propyl Paraben, Benzalkonium Chloride (0.01%w/v), Potassium Sorbate

V. METHODS OF PREPARATION OF NANOEMULSION

High-pressure equipment is the most efficient way to create nanoemulsions, which have an extremely small particle size range. In both laboratory and industrial settings, "high-pressure homogenization" and "micro fluidization" are the most often utilized techniques for creating nanoemulsions. Other techniques that can be used to prepare nanoemulsion include "Ultrasonification" and "In-situ emulsification."[5]

- High-Pressure Homogenization
- Microfluidization
- Spontaneous Emulsification
- Solvent Evaporation Technique
- Hydrogel Method

1. High-Pressure Homogenization:

Relating an altitudinous over a complex with an oil painting phase, waterless phase, and surfactant orco-surfactant is how this procedure is carried out. The homogenizer is used to help apply the pressure. Poor productivity and element deterioration that results in inordinate heat generation are some issues with homogenizers. With this fashion, only liquid oil painting in Water (O/ W) nanoemulsions with lower than 20 oil painting phases can be created; cream nanoemulsions with high density or hardness and mean drop compasses lower than 200 nm cannot. [6]

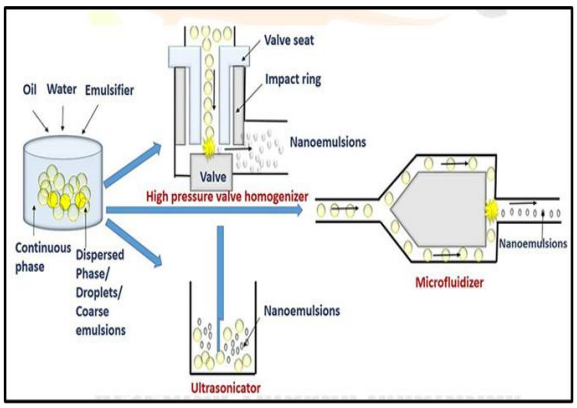

Fig:1. High-Pressure Homogenization

2. Micro fluidization:

The" MICRO FLUIDIZER" is a tool used in micro fluidization technology. The product is pushed into the commerce chamber, which is made up of bitsy channels called micro channels, using a high- pressure positive relegation pump (500 – 200 PSI). The yield travels via the microchannels and into the crash region, delivering truly small spots in the submicron pasture. An inline homogenizer is used to blend the two results (unctuous phase and waterless phase) and process them into a thick conflation. A micro fluidizer is used to further convert the coarse conflation into a stable nano conflation. [8]

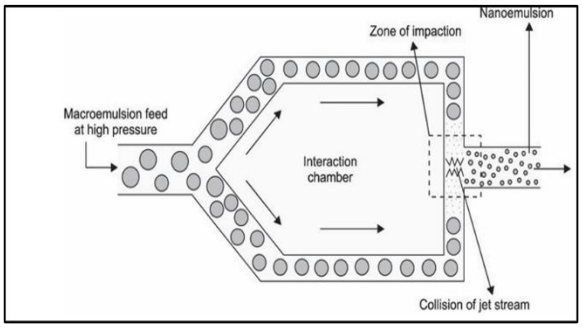

Fig.2. Micro fluidization

3. Spontaneous emulsification

It involves three main way-

a. Preparation of homogeneous organic result composed of oil painting and lipophilic surfactant in water miscible detergent and hydrophilic surfactant.
b. The organic phase is fitted in the waterless phase under glamorous stirring the o/w conflation was formed.
c. The water- miscible detergent is removed by evaporation under reduced pressure. [7]

4. Solvent Evaporation Technique

Solvent Evaporation fashion This fashion involves preparing a result of medicine followed by its emulsification in another liquid that'snon-solvent for the medicine. Evaporation of the detergent leads to rush of the medicine. Demitasse growth and flyspeck aggregation can be controlled by creating high shear forces using a high- speed stirrer [11].

5. Hydrogel Method:

It's analogous to solvent evaporation system. The only difference between the two styles is that the medicine detergent is miscible with the medicineanti-solvent. Advanced shear force helps crystal clear growth and Otwald growing. Other system used for Nanoemulsion medication is the phase inversion temperature fashion [9]

VI. TYPES OF NANOEMULSION

Both morphological and NEs are more likely to occur in three distinct forms depending on their compositional traits as demonstrated in the composition.

- Oil-in-water (O/W) nanoemulsions, where the oil is the continuous oil droplets are spread evenly throughout. the aquatic phase.
- Nanoemulsions of water in oil (W/O), where water is dispersed throughout the oil there are puddles of ter everywhere the oil phase.
- Nanoemulsions that are bi-continuous: These are available in two varieties. oil in water in oil (O/W/O) types - Here, Water serves as the dissolving agent, whereas oil functions as a solvent.in a dispersed manner. Water in oil is the second type.in water (O/W/O), where water serves as a dis the persion is transmitted through a medium that is dispersed and devoid of oil phase. [10]

VII. CONTENTS OF NANOEMULSIONS

(a) Aqueous phase

The characteristics of the aqueous phase, such as pH, ionic concentration, and electrolytes, have an impact on the size and stability of NEs. In testing the spontaneous Nano emulsification of NEs, the aqueous phase may be made up of phosphate buffered saline, plain water, simulated stomach fluid (pH 1.2), simulated intestinal fluid (pH 6.8), or Ringer's solution. pH is one of the aqueous phase's qualities that can have a big impact on how NEs behave in phases when a medication with a pH-dependent solubility is introduced to the system [12].

(b) Oil phase

Water is the second most crucial means of transportation.as a result of its ability to dissolve lipophilic drug molecules and boost absorption through the body's lipid layer. Oil extremely helpful for giving medications via lipophilic. because of its exceptional capacity for hydrophilic active substances ability to pass through cell membranes. The oil phase has an I'm the expansion of the surfactant's tail group area. Different oils are used to make NEs. [13]

S.No.	Oils	Chemical Name
1.	Capmul MCM	Glycerol monocaprylate
2.	Capryol90	Propylene glycol monocaprylate
3.	Captex 200	Propylene Dicaprylate
4.	Captex 355	Glyceryl Tricaorylate/Caprate
5.	Captex 8000	Glyceryl Tricaprylate
6.	Carbitol	Glycerol Triacetace
7.	Isopropyl Myristate	Myristic acid isopropyl ester
8.	Labrafac	Medium chain triglyceride
9.	Maisine 35-1	1-Monolinolein
10.	Myritol318	c8/cl0 triglyceride
11.	Peceol	Glyceryl Oleate
12.	Sefsol 218	Caprylic/ capric triglyceride
13.	Witepsol	90:10% w/w c-12 glyceride tri:diesters

Table:2. Types of oils used in nanoemulsions [13]

(c) Co-surfactants

To make these chemicals stronger, they are combined with surfactants. Due to its excellent fit between structures, the interfacial film found that the area was generally less stable. Co-surfacing If the surfactant is unable to lower the in, surfactants are used to create a stable interface between oil and water using interfacial tension The liquid crystalline phase is disrupted by the NE co-surfactant.by penetrating the surfactant monolayer and more enhances fluidity. [14] There are a wide variety of Co-surfactant use is widespread.

Name	Chemical name
Transcutol P	Diethylene glycol monoethyl ether
Ethylene glycol	Ethane 1.2 diol
Propylene glycol	1.2 propanediol

Table:3. Types of co-surfactants used in nanoemulsions. (14)

VIII. EVALUATION TESTS

1. Particle size analysis:

It is believed that the size of the droplet has an impact on how well the medication is absorbed; the smaller the droplet, the larger the interfacial surface area will be multiple factors affecting droplet size such as dilution volume, various media, and drug concentration are included in the provision for drug absorption method of loading and dispersing.

A particle size analyzer (Zetasizer) is used to measure the impact of dilution on droplet size in distilled water. The droplet size did not appear to alter upon a 1000-fold dilution, indicating that the nanoemulsion produced during dilution was able to maintain the drug in solution at a capacity that was 1000 times greater.

2. Surface charge measurements:

Emulsifiers not just function as a physical barrier but also by the creation of surface charges zeta the possibility of generating repulsive electricity forces between nearby oil droplets and this inhibits coalescence. more negative zeta the higher the potential and the net charge of the droplets, the higher the possibility, and the higher the zeta potential value, the more stable the emulsion. A low voltage, typically below -30 mV, indicates a high the extent of physical stability.

surface values for charging. The zeta potential and droplet size are the most important factors. representative parameters in the control emulsion as measured by Zetasizer, stability.

3. Percentage transmittivity research:

The prepared sample's percent transmittance nanoemulsion formulation Is? Determined using spectrophotometry. The composition has the following properties:

The highest percentage transmittance or very close to it. The composition is evident and 100% indicated. translucent. The mixture is diluted with 1 ml. analyzed at λ max after being treated with solvent 100 times using solvent as a blank.

4. Thermodynamic stability studies:

1. Heating and cooling cycle: Between six cycles refrigerator temperature between 4°C and 45°C wit storage at each temperature for at least 48 hour are examined. The formulations that are stable at these temperatures, the sample is centrifuged check.

2. Centrifugation: - The formulation that passed is centrifuged at 3500 rpm for 30 minutes. Those formulas that don't exhibit any phase The freeze-thaw stress test uses the separation procedure.

3. Freeze thaw cycle: - Three freeze thaw cycles between -21°C and 25°C, with storage at either end the temperature of the substance is maintained for at least 48 hours. Composition. The ones that passed the test The thermodynamic stress test is then continued for a dispersion test to determine the effectiveness of emulsification.

4. Transmission electron microscopy: To Pay attention to the form of the oil droplets in the The nanoemulsions are further distinct because of the following factors: TEM with negative staining.

5. Measuring viscosity: The viscosity of the substance is measured using this technique. The way formulations are determined is without dilution utilizing a Brookfield DV III ultra-RV with a V6.0 engine. rheometer with plate and cone at 25 ± 0.3.

IX. APPLICATIONS OF NANOEMULSION

Parenteral Delivery:

Parenteral authority (particularly via the intravenous passage) of medicines with limited solubility is a major problem in assiduity because of the extremely

equatorial quantum of medicine honestly redeemed to a targeted point.

Oral Delivery:
Nanoemulsion phrasings offer the several benefits over conventional oral expression for oral administration including increased immersion, bettered clinical energy, and dropped medicine toxin. thus, Nanoemulsion have been reported to be ideal delivery of medicines similar as steroids, hormones, diuretic and antibiotics.

Topical Delivery:
Ocular and Pulmonary Delivery:
In essence, medications are used topically to address eye conditions. o/w nanoemulsions have been studied for ocular delivery, to dissolve medications that are poorly soluble, to boost
absorption as well as to achieve a prolonged release profile. IPM was used as the oil phase and lecithin, propylene glycol, and PEG 200 as co-surfactants to create the pilocarpine-containing nanoemulsions. The compositions' low viscosity and refractive index made them suitable for use in ophthalmology. It has been reported that a fluorocarbon non-ionic surfactant stabilizes the creation of a water-in-HFA propellent nanoemulsion intended for pulmonary administration [15].

X. CONCLUSION

An oil and water nanoemulsion is a colloidal dispersion of two or more incompatible phases. As colloidal carriers for the targeted delivery of different anticancer medications, photosensitizers, neutron capture treatment agents, or diagnostic agents, they have recently attracted considerable attention. Drugs and food ingredients that are hydrophobic and have a high first pass metabolism suffer from limited bioavailability, which is efficiently addressed by nanoemulsion drug delivery devices. Researchers use high energy techniques to improve medication and bioactive food component delivery. With regard to composition factors, optimizations by selected parameter change or experimental designs allow for the conclusion that there is typically an ideal surfactant mixture composition, or HLB, where the larger the oil surfactant ratio, the larger the droplet size. Controlling numerous elements, such as the kind of oil phase, the methods employed, the process variables, and the addition of additives used across the inter phases of nanoemulsion formulation, could improve the formulation's stability. The physical and chemical instability of nanoemulsions restricts its uses. In this study, new approaches and factors for formulating successful nanoemulsions have been discussed in the hopes that they would serve as a model for future achievements in the field.

REFERANCES

[1] Anandharamakrishnan, C, 2014 Techniques for Nanoencapsulation of Food Ingredients, Springer

[2] Anton, N., Benoit, J.P., and Saulnier, P., 2008 Design and production of nanoparticles formulated from nano-emulsion templates-A review, Journal of Controlled Release, 128, 185-199.

[3] Ahuja A., Ali J., Baboota S., Faisal M., Shakeell F., Shafiq S., Stability evaluation of Celecoxib nanoemulsion containing Tween 80, Thai J Pharm Sci, 2008; 32: 4-9.

[4] Banker G., Lieberman H., Rieger M., Pharmaceutical dosage forms, Disperse systems, Marcel Dekker, 2002; 2:3: 339-40, 343-44.

[5] Bhatt P. and Madhav S., A Detailed review on nanoemulsion drug delivery system, International Journal of Pharmaceutical Sciences and Research 2011; 2:10: 2482- 2489.

[6] Wang Y. Preparation of nano- and microemulsions using phase inversion and emulsion titration methods. Master’s thesis. Massey University, Auckland, New Zealand. 2014.

[7] Singh Y, Meher JG, Raval K, Khan FA, Chaurasia M, Jain NK, et al. Nanoemulsion: concepts, development and applications in drug delivery. J Control Release. 2017. 252:28-49.

[8] Bouchemal K., Briancon S., Fessi H., Perrier E., Nano emulsion formulation using spontaneous emulsification: solvent, oil and surfactant optimization. International Journal of Pharmaceutics 2004; 280: 243.

[9] Guglielmini G., Nanostructured novel carrier for topical application, Clin Dermatol 2008; 26: 341-6.

[10] 8. Huabing C., Danrong D., Chengwen M., Dongsheng M., Jiangling W., Huibi X., Xiangliang Y., Hydrogel-thickened nanoemulsion system for topical delivery of lipophilic drugs, International Journal of Pharmaceutics 2008; 353: 272.

[11] Attwood D., Mallon C., Taylor C., Phase studies of oil-in water phospholipid microemulsions, Int. J. Pharm. 1992; 84: R5–R

[12] Sarker A, Shimu IJ (2015) Md. Riazul Haque Tuhin and Ali Asgher Raju. Nanoemulsion: An excellent mode for delivery of poorly soluble drug through different routes. Journal of Chemical and Pharmaceu tical Research 7(12): 966–976.

[13] Kale SN, Deore SL (2017) Emulsion Micro emulsion and nano emulsion: A review. Systematic Reviews in Pharmacy 8(1): 39–47. https://doi. org/10.5530/srp.2017.1.8

[14] Mushtaq A, Wani SM, Malik AR, Gull A, Ramniwas S, Nayik GA, Ercisli S, Marc RA, Ullah R, Bari A (2023) Recent insights into nanoemul sions: Their preparation, properties and applications. Food Chemis try: X 18: 100684.https://doi.org/10.1016/j.fochx.2023.100684

[15] Wilson RJ, Li Y, Yang G, Zhao CX (2022) Nanoemulsions for drug delivery. Particuology 64: 85–97. https://doi.org/10.1016/j.partic.2021.05.009