REVIEW ON NANOEMULSION: A VERSATILE APPROACH TO NOVEL DRUG DELIVERY

Priya Patel*, Chainesh Shah, Mansi Patel, Jigar Vyas, Umesh Upadhyay
Sigma Institute of Pharmacy, Bakrol, Vadodara- 390019.

ABSTRACT

Nanoemulsions are emulsions that are produced in nanometer sizes to enhance the delivery of pharmacological active substances. These are the thermodynamically stable isotropic systems in which an emulsifying agent, such as a surfactant and a co-surfactant, is used to combine two immiscible liquids into a single phase. Nanoemulsion typically has droplet sizes between 20 and 200 nm. A biphasic dispersion of two incompatible liquids, such as water in oil (W/O) or oil in water (O/W) droplets stabilised by an amphiphilic surfactant, is what is known as a nanoemulsion. These appear to be ultrafine dispersions with differential viscoelastic, visual, and drug loading properties that can support a variety of activities, including drug delivery.

KEYWORDS: Nanoemulsion, Microfluidization, globules

INTRODUCTION [1-3]

The future of cosmetics, diagnostics, pharmacological therapies, and biotechnologies all appear to be bright for the emerging class of dispersed particles known as nanoemulsions. Oil-in-water (o/w) emulsions with mean droplet diameters between 50 and 1000 nm are known as nanoemulsions. The typical range of droplet sizes is 100 to 500 nm. The particles can exist as water-in-oil or oil-in-water forms, depending on whether water or oil make up the centre of the particle. Mini-emulsion and sub-micron emulsion (SME) are interchangeable words. SMEs typically comprise 10–20% oil stabilised with 0.5–2% egg or soybean lecithin. Using a high-stress, mechanical extrusion procedure, phase into an aqueous phase Surfactants that are safe for human consumption and common food ingredients that have been designated as "Generally Recognized as Safe" (GRAS) by the FDA are used to create nanoemulsions. By combining water immiscible oil that is widely available, these emulsions are easily manufactured in large quantities. Miniemulsions, ultrafine emulsions, and submicron emulsions are other names for nanoemulsions. The size of droplets is determined by the surfactant phase structure (bicontinuous microemulsion or lamellar) at the inversion point caused by either temperature or composition, according to phase behaviour research. Studies on Nanoemulsions formation by the phase inversion temperature method have shown a relationship between minimum droplet size and complete solubilization of the oil in a microemulsion bicontinuous phase independently of whether the initial phase equilibrium is single or multiphase.

Advantages of Nanoemulsions over other dosage forms [4, 5]

1. Eliminates variability in absorption
2. Increases the rate of absorption.
3. Helps in solublizing lipophilic drug.
4. Provides aqueous dosage form for wa- ter insoluble drugs.
5. Increases bioavailability.
6. Various routes like topical, oral and intravenous can be used to deliver the product.
7. Rapid and efficient penetration of the drug molecule.
8. Helps in taste masking.
9. Provides protection from hydrolysis and oxidation as drug in oil phase in o/wemulsion
10. Less amount of energy required
11. Liquid dosage form increases patient compliance
12. Nanoemulsions are thermodynamically stable systems and the stability allows self-emulsification of the system whose properties are not dependent on the process followed.
13. Nanoemulsionscarry both lipophilic and hydrophilic compounds.
14. Use of Nanoemulsion as delivery systems improves the efficacy of a drug, allowing the total dose to be reduced and thus minimizing side effects.

Disadvantages of Nanoemulsion Based Systems [6, 7]

1. Use of a large concentration of surfactant and cosurfactants necessary for stabilizing the Nanodroplets.
2. Limited solubilizing capacity for high melt- ing substances.
3. The surfactant must be nontoxic for phar- maceutical applications.
4. Nanoemulsion stability is influenced by environmental parameters such as temperature and pH. These parameters change upon Nanoemulsion delivery to patients.

COMPONENTS OF NANOEMULSION [8-10]

Main three components of Nanoemulsions are

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

Colloidal dispersions known as nanoemulsions consist of an oil phase, aqueous phase, surfactant, and cosurfactants in the proper proportions. Nanoemulsions are based on low interfacial tension, in contrast to coarse emulsions micronized by external energy. A thermodynamically stable na- noemulsion spontaneously forms when cosurfactants are added, enabling this. Since the droplet size in the dispersed phase is typically below 140 nm, nanoemulsions are transparent liquids. They deliver messages.

There are various ways to deliver medications to patients, but topical administration of nanoemulsions has drawn a lot of attention. The mobility of the drug inside the vehicle, the release of the drug from the vehicle, and the permeation of the drug into the skin are the three key elements that affect transdermal permeation of pharmaceuticals. Thus, they outperform conventional topical preparations like emulsions

and gels in terms of transdermal drug delivery. Compared to nanoemulsions containing gel, which will enhance their viscosity and further reduce skin permeability, medicines move more easily in nanoemulsions. It has been established that nanoemulsions' higher transdermal flow is primarily a result of their strong drug solubilization capacity for both lipophilic and hydrophilic compounds. As a result, the skin experiences enhanced thermodynamic activity. They might have an impact on how easily a medicine penetrates the skin. In this situation, the nanoemulsion's constituent parts act as permeation promoters. Several substances included in nanoemulsions have been reported to enhance transdermal penetration by changing the stratum corneal structure. For instance, short chain alkanols are frequently employed to improve permeability. The lipid barrier in the stratum corneum is known to be disrupted by oleic acid, a fatty acid with one double bond in the chain structure. This occurs by the formation of distinct domains that obstruct the continuity of the multilamellar stratum corneum and may result in highly permeable pathways.

NANOEMULSION FORMULATION INFLUENCING FACTORS [11-13]

1. The most crucial component of the Nanoemulsion is the surfactant. They shouldn't create "micro-emulsions" phases of lyotropic liquid crystal. Phases that are typically utilised with the co-surfactant are systems with short chain alkanes, alcohols, water, and surfactants.
2. Appropriate composition is required to avoid Oswald ripening andthe dispersed phase should be highly insoluble in the dispersion medium.
3. The presence of excess surfactants enables new surface area of nanoscale to be rapidly coated during emulsification there by inhibiting induced coalescence.

THEORIES OF NANOEMULSION [14-18]

- **Monomolecular films**

By generating a monolayer of adsorbed molecules or ions at the interface and lowering interfacial tension, surfactant-type emulgents stabilise a nanoemulsion. Combinations of emulgents are preferred to single emulgents in contemporary practise. The mixture creates a complicated film at the interface by combining an emulgent that is mostly hydrophilic in the aqueous phase with a hydrophobic agent in the oily phase.

- **Multimolecular films**

Globules of scattered oil are encircled by multimolecular films made of hydrated lyophilic colloids. Surface tension of hydrated colloids and their capacity to produce robust, coherent multimolecular films are not significantly reduced. The emulsion's stability is improved by their propensity to make the continuous phase viscous.

- **Solid particulate films**

The emulgents forming particulate films are small solid particles that are wetted to some degree by both aqueous and non-aqueous liquid phases. They are concentrated at the interface where they produce a film around the dispersed globules thus preventing coalescence.

METHOD OF PREPARATION OF NANOEMULSION [19-25]

1. High Pressure Homogenization

A high pressure homogenizer must be used to prepare the nanoemulsion. This technique creates nanoemulsions with 10-100nm-sized particles. By applying significant turbulence and hydraulic shear to the product and driving the combination via a small inlet orifice at a high pressure (500 to 5000 psi), the dispersion of the (oily and aqueous phase) is achieved. The resulting particles have a monomolecular layer of phospholipides separating the liquid, lipophilic core from the surrounding aqueous phase.

The following process variables should be looked at to produce the optimum formulation:

- ✓ **Effect of Homogenization Pressure:** 100 to 150 bars should be the pressure. The resultant particle size decreases with increasing pressure.
- ✓ **No. of Homogenization cycles:** The higher the homogenization cycles the smaller is the particle size ob- tained. The cycles are carried out in 3, 4 or 10 cycles. The number of cycles is analyzed by polydispersity index of drug after each cycle.

Advantages

1. Ease of scale-up and little batch-to- batch variation
2. Narrow size distribution of the nano- particulate drug.
3. Flexibility in handling the drug quality.
4. Effectively used for thermolabile sub- stances.

Disadvantages

1. High energy consumption
2. Increase in temperature of emulsion during processing

2. Microfluidization

A tool called a microfluidizer is used in the mixing process known as microfluidization. This device pushes the product through an interaction chamber made up of tiny channels known as "micro channels" using a high-pressure positive displacement pump (500 to 20000 psi). The product flows through the microchannels and onto the area of impingement, producing small particles with a size range of less than one micron. A coarse emulsion is produced by combining the two solutions (the aqueous phase and the oily phase) and processing them in an inline homogenizer. To create a stable nanoemulsion, the coarse emulsion is further treated in a microfluidizer. The interaction chamber microfluidizer is used to repeatedly circulate the coarse emulsion through until the desired particle size is achieved. After the big droplets are removed from the bulk emulsion using a filter under nitrogen, a homogenous nanoemulsion is produced. Until the appropriate droplet size is reached, the premixed emulsion is periodically circulated via the microfludizer.

3. Ultrasonication

Ultrasonic sound frequency can be used to create nanoemulsions and reduce globule size. Utilizing a constant amplitude sonotrode at system pressures higher than ambient is another strategy. It is common knowledge that when external pressure rises, the cavitation threshold in an ultrasonic field rises as well, leading to a reduction in bubble formation. However, raising the external pressure also raises the

cavitation bubbles' collapse pressure. This indicates that when cavitation occurs, the collapse of the bubbles is stronger and more severe than when the pressure is at atmospheric levels. These variations in the navigational intensity can be directly linked to variations in the power density since cavitation is the most significant process of power loss in a low frequency ultrasonic system. The system also uses a water jacket to control the temperature to optimum level.

4. Phase inversion method

Using chemical energy generated by phase changes caused by the emulsification process, this approach produces fine dispersion. When the emulsion's composition is changed while the temperature is held constant, or the opposite is true, a phase transition results.

5. Spontaneous Emulsification

There are three main steps.

• Making a homogenous organic solution using a hydrophilic surfactant and a water-miscible solvent that contains oil and a lipophilic surfactant.

The water-miscible solvent was transported by evaporation under reduced pressure. The organic phase was injected into the aqueous phase under magnetic stirring, resulting in an o/w emulsion.

6. Solvent Evaporation Method

This method entails making a medication solution, then emulsifying it in a different liquid that isn't the drug's solvent. Precipitation results from the solvent evaporating. Crystal growth and particle aggregation can be controlled by creating high shear forcing high-speed stirrer.

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 [26-29]

The distinctive characteristics and effectiveness of nanoparticles as medication delivery systems result directly from their physicochemical characteristics. As a result, it is eager to comprehend and identify them in order to define them as its behaviour. A thorough knowledge enables rational particle design, formulation development, and process troubleshooting in addition to permitting prediction of in vivo performance. It will have qualities like testing for thermodynamic stability. Globule size distribution, assessment of dilution stability transmittance. In vitro testing and zeta potential. In addition, it should be examined for pH, conductivity, refractive index, and other factors like 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 Solubilisation

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

2. Dilutability Test

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

3. Conductance Measurement

Since water is the internal or dispersal phase of O/W nanoemulsions but not W/O, the former are highly conducting. Electrical conductivity tests are very helpful in identifying the continuous phase's characteristics and spotting phase inversion events. In some W/O Nanoemulsion systems, a sudden increase in conductivity was seen at low volume fractions. This behaviour was understood to be an indicator of 'percolative behaviour' or an ion exchange between droplets prior to the creation of bicontinuous structures. Dielectric measurements are an effective tool for examining the dynamic and structural characteristics of Nanoemulsion systems.

4. Dynamic Light-Scattering measurements

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

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

By measuring the interfacial tension, it is possible to investigate the development and characteristics of nanoemulsions. Phase behaviour and extremely low interfacial tension levels are connected especially the presence of the middle- or surfactant-phase balance between aqueous and oil phases in nanoemulsions.

It is possible to quantify the extremely low interfacial tension using a spinning-drop instrument. When a drop of the low-density phase is rotated in a cylinder-shaped capillary that is filled with the high-density phase, the form of the drop is measured to determine the interfacial tensions.

8. Viscosity measurement

Temperatures using Brookfield type rotary viscometer. The sample room of the instrument The viscosity of Nanoemulsions of several compositions can be measured at different shear rates at different must be maintained at 37±0.2°C by a thermo bath, and the samples for the measurement are to be immersed in it before testing.

9. pH

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

10. Refractive Index (Aubrun et al., 2004)

The refractive index, n, of a medium is defined as the ration f the speed, c, of a wave such as light or sound in a reference medium to the phase speed, vp, of the wave in the medium. n=c/vp; It was determined using an Abbes type refractrometer (Nirmal International) at 25±0.5°C.

11. Transmission Electron Microscopy (TEM)

The nanoemulsion's morphology and structure were examined using transmission electron microscopy. The shape and size of the nanoemulsion droplets were revealed using a combination of diffraction modes and bright field imaging at escalating magnification. The observations were carried out by dropping a drop of the nanoemulsion directly onto the grid of holes in the holey film and watching it dry.

12. In Vitro Skin Permeation Studies

Keshary Chien-diffusion cells were used to conduct in vitro skin permeation investigations. It was carried out using abdominal skins made from male rats weighing 25010 grammes, and it had 12 diffusion cells and a water bath that circulated. Vertical diffusion cells' donor and receiver chambers were separated by the skins. Fresh water containing 20% ethanol was poured into the receiver chambers. The solution in the receiver chambers was constantly agitated at 300 rpm while the receiver chambers were heated to a temperature of 37ºC. The donor chamber was filled with the compositions. 0.5 ml of the solution in the receiver chamber was taken out for GC analysis at 2, 4, 6, and 8 hours and immediately replaced with a fresh solution of the same volume. Three samples were run for each. To determine the overall amounts of medicines penetrated at each time interval, cumulative adjustments were done. Plots were made as a function of time showing the total amounts of medication that passed through the skin of rats. The slope of the linear part of the cumulative amount permeated through the rat skins per unit area vs time plot was used to compute the steady-state drug permeation rates via rat skins.

13. Studies on thermodynamic stability

Following stress tests, the thermodynamic stability of drug-loaded nano-emulsions was observed as follows:

- ✓ **Cycle of Heating and Cooling:** Six cycles of nanoemulsion formulations between refrigerator temperature (4°C) and 45°C were performed. The centrifugation test was then performed on the stable formulations.
- ✓ **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.
- ✓ **Freeze Thaw Cycle:** In this the formulation were subjected to three freeze thaw cycles between 21°C and +25°C kept under standard laboratory conditions. These studies were performed for the period of 3 months.

APPLICATION OF NANOEMULSIONS [30-32]

❖ Nanoemulsions in Cosmetics

Recently, nanoemulsions have grown in significance as prospective delivery systems for cosmetics and for the optimal dispersion of active substances in specific skin layers. Nanoemulsions are preferable to liposomes for the transport of lipophilic substances because of their internal lipophilicity. Because nanoemulsions do not naturally cream, silt, flocculate, or coalesce as macro emulsions do, they are suitable for use in cosmetics. Using high-energy machinery during manufacture can frequently prevent the addition of potentially irritating surfactants.

As possible vehicles for the regulated delivery of cosmetics and the optimal dispersion of active chemicals in specific skin layers, nanoemulsions have drawn a lot of attention in recent years for use in personal care products.

❖ Antimicrobial Nanoemulsions

Oil-in-water droplets called antimicrobial nanoemulsions have a size between 200 and 600 nm. They are made of oil and water and are stabilised with alcohol and surfactants. the against fungus (such as Candida, Dermatophytes), bacteria (such as E. coli, Salmonella s, and S. aureus), enveloped viruses (such as HIV, Herpes simplex), and spores (e.g. anthrax). Thermodynamic forces cause the nanoemulsion particles to bind to lipid-containing organisms.

The pathogen's anionic charge and the cationic charge of the emulsion are electrostatically attracted to one another, facilitating this fusion. A portion of the energy held in the emulsion is released when enough nanoparticles combine with the pathogens. The pathogen's lipid membrane is made unstable by the active ingredient and the energy produced, which causes cell lysis and death. Additional germination boosters are added to the emulsion in the event of spores. The germinating spores are vulnerable to the antimicrobial effects of the nanoemulsion once germination has begun. The nanoemulsion can therefore attain a degree of topical antibacterial activity previously only possible with systemic medicines.

❖ As A Mucosal Vaccine

Recombinant proteins or inactivated organisms are delivered to a mucosal surface using nanoemulsions in order to elicit an immune response. Clinical studies can be conducted on the initial applications, an influenza vaccine and an HIV vaccine. Proteins applied to the mucosal surface become adjuvants thanks to the nanoemulsion, which also makes it easier for antigen-presenting cells to take them up. The proof of concept in animal trials for other vaccinations, such as those for Hepatitis B and anthrax, is still being worked on Recombinant HIV gp120 antigen applied intranasally to mice and guinea pigs resulted in strong serum anti-gp120 IgG as well as bronchial, vaginal, and serum anti-gp120 IgA in the mice.

In addition to having considerable neutralising activity against two clade-B laboratory strains of HIV (HIVBaL and HIVSF162) and five primary HIV-1 isolates, the serum from these animals showed antibodies that cross-reacted with heterologous serotypes of gp120. Nasal vaccination in nanoemulsion also generated systemic, Th1-polarized cellular immune responses, according to analyses of gp120-specific CTL proliferation, INF-g induction, and predominance of anti-gp120 IgG2 subclass antibodies. This study makes the case for further research into nanoemulsion's potential as a mucosal adjuvant for

multivalent HIV vaccinations. Despite the availability of secure and reliable preventive vaccinations, hepatitis B virus infection remains a significant worldwide health risk.

In two recent studies, a novel method for immunising against a number of infectious illnesses that uses an oil-based emulsion administered by the nose rather than needles has demonstrated its ability to induce a potent immune response against smallpox and HIV. The ability to develop mucosal immunity may be crucial for HIV defence. According to the study, the nanoemulsion HIV vaccine can produce cellular immunity, mucosal immunity, and antibodies that can neutralise different HIV viral isolates. One of the main binding proteins being investigated in various HIV vaccine strategies is gp120, a protein that the team uses.

- **Nanoemulsion as Non-Toxic Disinfectant Cleaner**

EnviroSystems, Inc. has created a ground-breaking nontoxic disinfectant cleaner for use in commercial sectors such as healthcare, hospitality, travel, food processing, and military applications that kills tuberculosis and a wide range of viruses, bacteria, and fungi in 5–10 minutes without any of the risks associated with other disinfectant types. Warning labels are not required for the product. It does not irritate the eyes and is safe to consume, inhale, and absorb via the skin. The disinfection formulation uses tiny amounts of the active component, PCMX, in the form of oil droplet nanospheres floating in water to generate a NE (parachlorometaxylenol). The surface charges on the nanospheres effectively pierce the surface charges on the membranes of microorganisms, breaking through them much like an electric fence. The formulation enables PCMX to target and penetrate cell barriers as opposed to "drowning" cells. There are no hazardous effects on people, animals, or the environment because PCMX is effective at concentration levels 1-2 orders of magnitude lower than those of conventional disinfectants. Other microbial disinfectants need to surround pathogen cell walls with high concentrations of their respective active ingredients in order for them to breakdown, thus "drowning" the pathogens in the disinfectant solution. The mixture is a multipurpose cleaner and disinfectant that may be used on any hard surface, including furniture, counters, walls, fixtures, and floors. Now that one product can replace many others, stocks are reduced and precious storage space is saved.

- **Nanoemulsions in Cell Culture Technology**

Cell cultures are employed for in vitro tests or to make biological substances like recombinant proteins or antibodies. Blood serum or a number of designated compounds can be added to the culture medium to improve cell development. Better uptake of oil-soluble nutrients in cell cultures, improved growth and vitality of cultured cells, and improved cell viability are all benefits of employing nanoemulsions in cell culture technologies allowing oil-soluble drug toxicity investigations in cell cultures.

- **Nanoemulsion in Cancer Therapy and Targeted Drug Delivery**

For use in cancer neutron-capture therapy, the effects of the formulation and particle composition of gadolinium (Gd)-containing lipid nanoemulsion (Gd-nanoLE) on the biodistribution of Gd following its intravenous (IV) injection in D1-179 melanoma-bearing hamsters were assessed. According to biodistribution statistics, Brij 700 and HCO-60 increased Gd's concentration in tumours and prolonged its time in the blood. The majority of the drug's localization after dermal administration was in deeper skin

layers, with little systemic escape. This has resulted in a 70.62% absolute bioavailability. D-tocopheryl polyethyleneglycol 1000 succinate and labrasol would have helped to increase the peroral bioavailability of PCL by inhibiting P-glycoprotein efflux. This study offers concrete proof of PCL, a high-molecular-weight, lipophilic drug dermals localisation. Furthermore, the peroral bioavailability has increased dramatically to more than 70% thanks to the nanoemulsion formulation. The created nanoemulsion formulation proved secure and efficient for PCL delivery via cutaneous and oral routes. A topoisomerase-I inhibitor, camptothecin works against a variety of malignancies. However, due to its insolubility, instability, and toxicity, its clinical applicability is constrained.

❖ **Nanoemulsion in the Treatment of Various Other Disease Conditions**

The topical diclofenac nanoemulsion cream was created by Pharmos (a US-based company) as a potential treatment for osteoarthritis (OA) pain. Over 30 million Americans suffer from the painful condition of OA, which is the most common cause of physical disability in adults, primarily the elderly. Another option for treating soft tissue injuries, sprains, and strains is topical diclofenac. According to estimates, 20% of OA patients do not receive treatment, primarily because COX-2 inhibitors and oral NSAIDs have cardiovascular risks and gastrointestinal side effects. For these patients, a topical NSAID with an enhanced safety profile that may provide effective pain management at the injury site may replace oral medications. There are no topical NSAIDs that have been licenced for the treatment of OA in the USA. The effective solvent-free topical carrier used by Pharmos' NE technology is based on stable, submicron oil-in-water emulsion particles with mean droplet sizes between 100 and 200 nm that are uniformly disseminated in an aqueous phase. The relatively high percentage of total particle volume occupied by the interior hydrophobic oil core of the droplets is one of the distinctive features of the nanoemulsion technology. Compared to other lipoidal carriers like liposomes, this offers strong solubilization capability for lipophilic substances. For the purpose of producing creams with the necessary semisolid consistency for application to the skin, nanoemulsion thickening employs chemicals that impart viscosity. This new topical nanovehicle is a viable candidate for efficient transcutaneous administration of lipophilic medicines due to its skin penetrating characteristics and minimal irritancy of the solvent-free nanoemulsion delivery method.

❖ **Nanoemulsion Formulations for Improved Oral Delivery of Poorly Soluble Drugs**

In order to increase the oral bioavailability of hydrophobic medicines, nanoemulsion formulations were created. One hydrophobic medication was used as a model: paclitaxel. Pine nut oil was used as the internal oil phase, egg lecithin as the main emulsifier, and water as the external phase to create O/W nanoemulsions. The emulsions were given a positive and a negative charge using stearylamine and deoxycholic acid, respectively. The formed nanoemulsions ranged in zeta potential from +34 mV to 245 mV and had particles between 90 and 120 nm in size. When given orally, paclitaxel was found in much higher concentrations in the systemic circulation when given in the nanoemulsion than in the control aqueous solution. The study's findings imply that nanoemulsions are innovative formulations with promise for improving the oral bioavailability of hydrophobic medicines.

❖ **Nanoemulsions as a Vehicle**

The generated nanoemulsions offer a significant deal of potential for transdermal drug administration of aceclofenac, according to findings from in vitro and in vivo studies. The ketoprofen-containing system's nanoemulsion demonstrated a high level of stability. When compared to the control, ketoprofen-loaded nanoemulsions increased the rate at which drugs penetrated mouse skin in vitro.

❖ **Self-Nanoemulsifying Drug Delivery Systems**

Self-nanoemulsifying drug delivery systems: formulation development, in vitro transport investigation, and in vivo oral absorption study for oral delivery of protein medicines. In order to distribute protein therapeutics non-invasively, a self-nanoemulsifying drug delivery system (SNEDDS) was developed. In order to create SNEDDS, an experimental design was used. Beta-lactamase fluorescently tagged model protein called BLM was loaded into SNEDDS using the solid dispersion method.

CONCLUSION

Formulations using nanoemulsions have a number of benefits for the administration of biological, therapeutic, or diagnostic substances. For more than 40 years, clinics have been using nanoemulsions as fluids for whole parenteral feeding. Nanoemulsions are typically used to deliver aqueous insoluble medications, but more recently, colloidal carriers for the targeted delivery of certain anticancer medications, photo sensitizers, neutron capture treatment agents, or diagnostic agents have drawn attention.

REFERENCES

1. Thakur Nishi, GargGarima, Sharma P.K. and Kumar Nitin. Nanoemulsions: A Review on Various PharmaceuticalApplicationsGlobal Journal of Phar- macology. 2012;6 (3): 222-225.
2. TheajRavi,U Prakash andThiagarajaP. Irritancymake it a suitable carrier for the Nanoemulsions for drug delivery through different transdermal delivery of the drugs in the routes. Research in Biotechnology.2011; 2(3): 01-13.
3. SharmaN, BansalM. and Visht S.Nanoemulsion: A new concept of delivery applicationof nanoemulsion. System.2010;1(2): 2-6.
4. Devarajan V and Ravichandran V: Nanoemulsions: As Modified Drug De- livery Tool. International Journal of Comprehensive Pharmacy. 2011; 4 (01):1-6.
5. Shah P, Bhalodia D.Nanoemulsion: A Pharmaceutical Review. Sys Rev Pharm. 2010; 1(1):24-32.
6. Trotta M, Influence of phase transfor- mation on indomethacin release from microemulsions. J Control Re- lease.1999; 60:399-405.
7. Figueroa Alvarez, MJ and Blanco- Méndez, Transdermal delivery of me- thotrexate: iontophoretic delivery from hydrogels and passive delivery from microemulsions. Int J Pharm.2001; 215: 57-65.
8. Bhatt P and Madhav S: A Detailed Review on Nanoemulsion Drug Deli- very System. International Journal of Pharmaceutical Sciences and Re- search. 2011; 2(10):2482-2489.
9. Ahuja A, Ali J, Baboota S, Faisal MS, Shakeell F, Shafiq S. 2008. Stability evaluation of Celecoxib nanoemulsion containing Tween 80. Thai Journal of Pharmaceutical Sciences, 32:4–9.

10. Anton N, Saulnier P. 2008. Design and production of nanoparticles formulated from nano-emulsion templates-a review. Journal of Controlled Release, 128:185-199.
11. Asthana S, Jaiswal AK, Gupta PK, Pawar VK, Dube A, MK Chourasia. 2013. Immuno adjuvant chemotherapy of visceral leishmaniasis in hamsters using amphotericin B-encapsulated nanoemulsion template-based chitosan nanocapsules. Antimicrobial Agents and Chemotherapy, 57:1714–1722.
12. Aubrun OS, Simonnet JT, Alloret FL. 2004. Nanoemulsions: a new for skincare products. Journal of Colloid and Interface Science, 108-109:145-149.
13. Bawa R, Audette GF, Reese B. 2016. Handbook of Clinical Nanomedicine: Law, Business, Regulation, Safety, and Risk, CRC Press,
14. Buscall R, Davis SS, Potts DC. 1979. The effect of long-chain alkanes on the stability of oil-in-water emulsions, the significance of ostwald ripening. Colloid and Polymer Science, 257:636–644.
15. Capek I. 2004. Degradation of kinetically-stable o/w emulsions.
16. Advances in Colloid and Interface Science, 107:125–155.
17. Charles L, Anthony A. 2011. Current state of Nanoemulsion: A review. Avaliable from:http://www.scirp.org/2011.
18. D'Souza S. 2014. A Review of In Vitro Drug Release Test Methods for Nano-Sized Dosage Forms. Advanced Pharmaceutical Bulletin, 1-12.
19. Devarajan V, Ravichandran V, 2011. Nanoemulsions: As Modified Drug Delivery Tool. International Journal of Comprehensive Pharmacy, 4(01):1-6.
20. Ganta S, Amiji M. 2009. Coadministration of paclitaxel and curcumin in nanoemulsion formulations to overcome multidrug resistance in tumor cells. Molecular Pharmaceutics, 6:928–939.
21. Ganta S, Sharma P, Paxton JW, Baguley BC, Garg S. 2010. Pharmacokinetics and pharmacodynamics of chlorambucil delivered in long- circulating nanoemulsion. Journal of Drug Targeting, 18:125–133.
22. Gasco MR, Gallarate M, Pattarino F. 1991. In vitro permeation of azelaic acid from viscosized mic roemulsions. Inte rna t i on al Jo urnal of Pharmaceutics, 69:193–196.
23. Guglielmini G. 2008. Nanostructured novel carriers for topical application. Clinics in Dermatology, 26:326- 331.
24. Hadgraft J. 2001. Skin, the final frontier. International Journal of Pharmaceutics, 224:1–18.
25. Hak S, Helgesen E, Hektoen HH, Huuse EM, Jarzyna PA, Mulder WJ, Haraldseth O, Davies L, Cde. 2012. The effect of nanoparticle polyethylene glycol surfacedensity on ligand-directed tumor targeting studied in vivo by dualmodality imaging. ACS Nano 6: 5648–5658.
26. Haskell R. 2012. Physical Characterization of Nanoparticles. Nanopart tech drug delivery. 159:126- 132.
27. Higuchi WI, Misra J. 1962. Physical degradation of emulsions via the molecular diffusion route and the possible prevention. Journal of Pharmaceutical Sciences, 51:459-466.

28. Huang H, Yu Q. 2012. Improving the oral bioavailability of curcumin using novel organogel-based nanoemulsions. Journal of Agricultural and Food Chemistry, 60:5373–5379.
29. Ichikawa, H., Watanabe, T., Tokumitsu, H., & Fukumori, Y. (2007). Formulation considerations of gadolinium lipid nanoemulsion for intravenous delivery to tumors in neutron-capture therapy. Current drug delivery, 4(2), 131-140.
30. 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.
31. Fang, J. Y., Hung, C. F., Hua, S. C., & Hwang, T. L. (2009). Acoustically active perfluorocarbon nanoemulsions as drug delivery carriers for camptothecin: drug release and cytotoxicity against cancer cells. Ultrasonics, 49(1), 39-46.
32. Kumar, M., Misra, A., Babbar, A. K., Mishra, A. K., Mishra, P., & Pathak, K. (2008). Intranasal nanoemulsion based brain targeting drug delivery system of risperidone. International journal of pharmaceutics, 358(1-2), 285-291.