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A REVIEW REPORT ON NANOEMULSION: FORMULATION, PROPERTIES AND POTENTIAL APPLICATIONS

Ayush Sidhu, Vishal Singh, Vishakha, Anjana Devi*
School of Pharmacy, Career Point University Bhoranj (Tikker - Kharwarian),
Hamirpur, Himachal Pradesh 176041, India

ABSTRACT

Nanoemulsions are colloidal dispersion systems that are thermodynamically stable and consist of two immiscible liquids that are mixed with emulsifiers (surfactants and co-surfactants) to form a single phase. Nanoemulsions have been extensively studied as drug delivery systems. This review aims to provide consolidated information on different formulation and characterization techniques that have been developed for nanoemulsions. Nanoemulsions are formulated using two different methods, the persuasion method, and the brute force method. The thermodynamic and high kinetic stability, alongside the tiny droplet size of nanoemulsions, have fueled their rapid development as a system for the delivery of bioactive substances/drugs in cosmetics and dermatological formulations. The composition and the manufacturing technique largely determine the quality of nanoemulsions. They are mainly aimed at high performance, product distribution to consumers, as well as the prospect of mass production. However, formulators face certain limitations, particularly regarding the diffusion of active ingredients into human skin. This overview describes the common techniques that have been used by formulators in recent years to produce nanoemulsions as end products for use in cosmeceuticals. Various characterization techniques for nanoemulsions include the determination of entrapment efficiency, particle size, polydispersity index, zeta potential, characterization by differential scanning calorimetry, Fourier transforms infrared spectroscopy, and transmission electron microscopy. Nanoemulsions are further evaluated by in vitro drug release, in vitro permeation, stability and thermodynamic stability, durability, dispersibility, viscosity, surface tension, frictional strength, refractive index, percent transmittance, pH, and osmolarity are examined.

Keywords*:* Nanoemulsion, Refractive index, Properties, Emulsion.

INTRODUCTION

Nanoemulsions are submicron-sized colloidal particle systems considered to be thermodynamically and kinetically stable isotropic dispersions consisting of two immiscible liquids such as water and oil stabilized by an interfacial film composed of a suitable surfactant and co-surfactant to form a single phase to build. Several surfactants with different properties (ionic or nonionic) have been used in such nanoemulsions. The most widely used among them were nonionic surfactants (sorbitan esters, polysorbates), anionic surfactants (potassium laurate, sodium lauryl sulfate), cationic surfactants (quaternary ammonium halide), and zwitterionic surfactants. (quaternary ammonium halide). Early nanoemulsions were oil-in-water (O/W) type emulsions with an average droplet diameter ranging from 50 to 1000 nm. B. O/W type (oil is dispersed in the aqueous phase), water-in-oil (W/O) type (water is disseminated in the oil phase), and bicontinuous. (Microdomains of water and oil are distributed within the system). Much research has focused on the production of nanoemulsions by various methods, including high-energy and low-energy methods. When formulating nanoemulsions, high energy consumption is the main limitation with methods such as micro fluidization, high-pressure homogenization (HPH), and ultrasonication [9]. Conversely, low-energy processes, H. Phase transition temperature, phase inversion composition, microemulsion dilution, and D-phase emulsification process, significantly less energy to formulate nanoemulsions Phase transition temperature, phase inversion composition, microemulsion dilution, and D-phase emulsification process consume much less energy. Several characterization methods are used to determine the properties of the formulated nanoemulsion.

These characterization techniques examine droplet size, shape, rheology, and system-stabilizing variables such as conductivity, pH, and zeta potential. Although nanoemulsions are kinetically stable, phase separation can occur through destabilization mechanisms such as flocculation, coalescence, Ostwald ripening, and creaming. To solve the problem of unstable nanoemulsions, it is necessary to control the influence of Ostwald ripening. Ostwald ripening causes the continuous phase evolution of larger oil droplets from smaller ones. A thorough analysis of the influence of variables such as temperature and nanoemulsion composition on destabilization rates was also performed. The current review addresses the use of low-energy techniques and optimization research for the application of nanoemulsions.

ADVANTAGES OF NANOEMULSIONS OVER OTHER DOSAGE FORMS

- Eliminates fluctuations in absorption.
- The absorption rate is increased.
- By assisting in the solubilization of lipophilic drugs.
- Less energy is required. Patient compliance is improved by liquid dosage forms.
- Nanoemulsions are thermodynamically stable systems that allow the system to emulsify itself as its properties are independent of the method used.
- Nanoemulsions transport substances that are both hydrophilic and lipophilic.

- The use of nanoemulsion as a drug delivery system increases the potency of a drug, which can reduce the overall dose and minimize side effects.

METHODS OF PREPARATION OF NANOEMULSIONS

The drug must be dissolved in the oil and water phase of the lipophilic nanoemulsion before being mixed with a co-surfactant and added slowly with gradual stirring until the system is transparent. Pseudo-ternary phase diagrams are used to calculate the amount of surfactant and co-surfactant to add and the percentage of oil phase that can be entrapped. The necessary size range for the dispersed beads can then be achieved through the use of ultrasonic devices and high-pressure homogenizers. It is then given time to equalize. A gelling agent may be added to the above nanoemulsion to produce a gel. The most popular gelling agents are carbomers (crosslinked polyacrylic acid polymers).

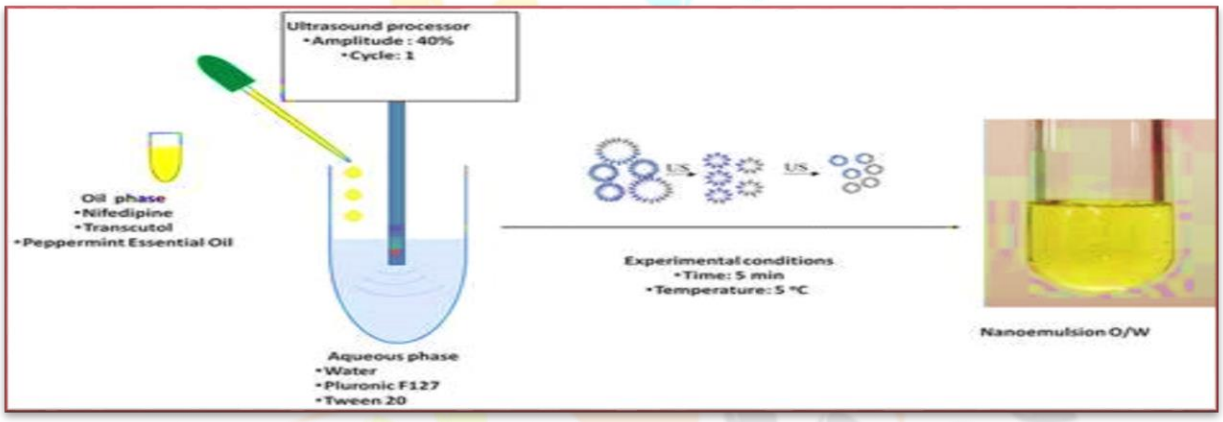

FIG: PREPARATION OF NANOEMULSIONS

FORMULATION OF NANOEMULSION

SCREENING OF EXCIPIENTS

By dissolving an excess amount of the drug in minute amounts of the selected oils, surfactants, and co-surfactants and mixing them with a vortex mixer, the solubility of the drug in various oils, surfactants, and co-surfactants is determined. The solubility of a substance can also be determined using a mixture of oils. The mixtures are allowed to equilibrate at room temperature in an isothermal shaker. Samples from the shaker are removed and centrifuged. The supernatant is filtered using a membrane filter with a pore size of 0.45 µm. HPLC or UV spectrophotometers are used to measure the drug concentration in each oil, surfactant, co-surfactant, and combination of oils at their respective peak levels.

HIGH-PRESSURE HOMOGENIZATION

A high-pressure homogenizer must be used to prepare the nanoemulsion. This technique produces nanoemulsions with 10–100 nm particles. The dispersion of (oily and aqueous phases) is achieved by forcing their mixture at high pressure (500 to 5000 psi) through a small inlet port, subjecting the product to significant turbulence and hydraulic shear, creating extremely thin emulsion particles. The resulting particles have a monomolecular layer

of phospholipids that separates their liquid, lipophilic core from the surrounding aqueous phase. The following process variables should be considered to obtain the optimal formulation.

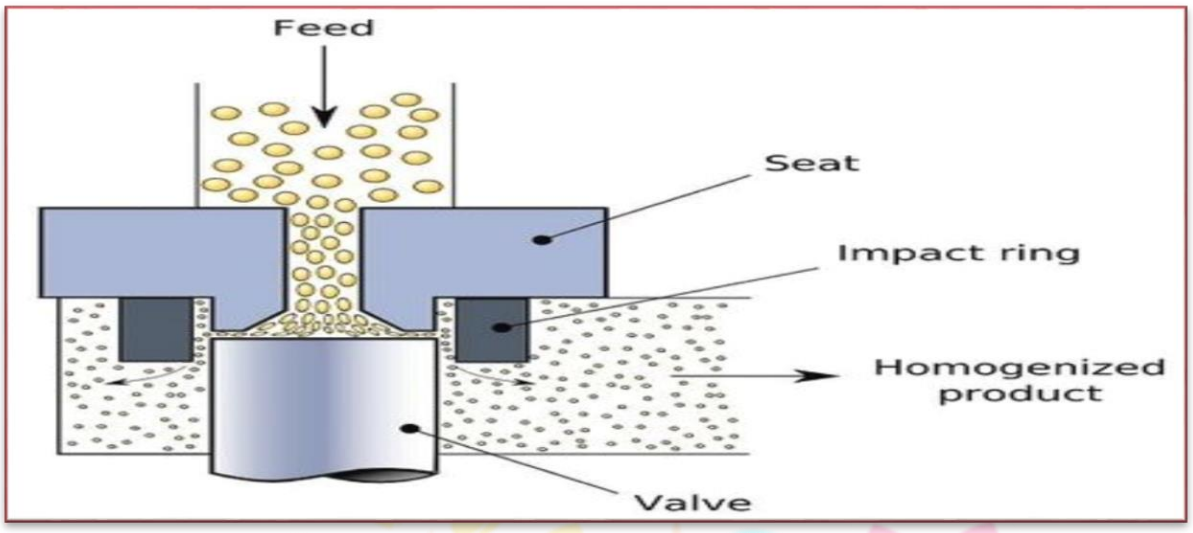

FIG: HIGH-PRESSURE HOMOGENIZATION

HOMOGENIZATION PRESSURE'S IMPACT

- It needs to be between 100 and 150 bars.
- The resultant particle size decreases with increasing pressure.

INSTANCES OF HOMOGENIZATION

The size of the obtained particles decreases with increasing homogenization cycles. 3, 4, or 10 cycles can be used to complete the cycles. After each cycle, the polydispersity index of the medication is used to calculate the number of cycles.

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 termed "micro-channels" using a high-pressure positive displacement pump (500 to 20000 psi). The product runs through the microchannels and onto the impingement area, producing submicron-sized fine particles. 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.

A consistent nanoemulsion is produced by filtering the bulk emulsion through a filter placed under nitrogen to remove big droplets. The prepared emulsion is repeatedly passed through the microfluidizer until the desired droplet size is obtained.

TECHNIQUE FOR SOLVENT EVAPORATION

In this method, a drug solution is made and then emulsified in another liquid that is not the drug's solvent. The precipitation of the drug results from the evaporation of the solvent. High shear forces generated by high-speed stirrers can be used to control crystal formation and particle aggregation.

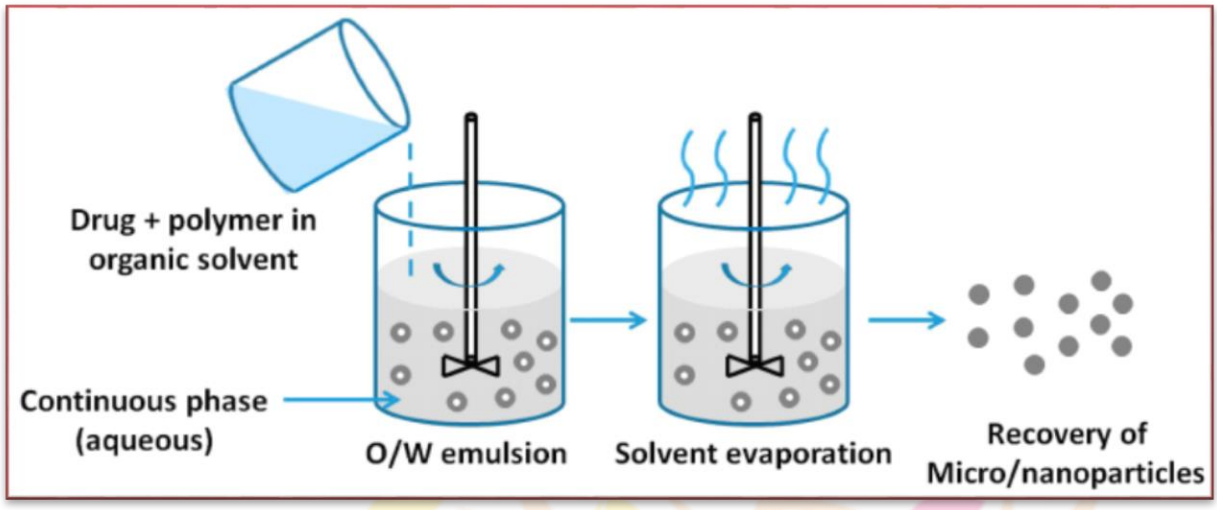

FIG: TECHNIQUE FOR SOLVENT EVAPORATION

PHASE INVERSION TECHNIQUE

- This technique uses chemical energy from phase transitions caused by the emulsification pathway to achieve fine dispersion.
- The phase transition is produced by changing the composition of the emulsion while the temperature remains the same or vice versa.

HYDROGEL METHOD

It is comparable to the process of solvent evaporation. The fact that the drug-solvent and drug-anti-solvent are miscible is the only difference between the two techniques. More shear inhibits Ostwald ripening and crystal development.

NANOEMULSIONS' PHYSICOCHEMICAL CHARACTERISATION

THE SOLUBILIZATION OF DYE

A water-soluble dye is dispersible in the O/W bead but solubilized in the aqueous phase of the W/O bead. An oil-soluble dye is dispersible in the w/o bead but is solubilized in the oil phase of the o/w bead.

TEST FOR DURABILITY

O/W nanoemulsions undergo phase inversion in O/W since they are diluted with water, but not w/o.

NANOEMULSION MEASUREMENTS OF DYNAMIC LIGHT SCATTERING

A neon laser with a wavelength of 632 nm is used in a dynamic light scattering spectrophotometer to perform the DLS measurements, which are performed at 90 degrees. The instrument's built-in computer is used to process the data.

POLYDISPERSITY INDEX

The mean diameters and the polydispersity index of the samples were determined using photon correlation spectroscopy. The A He-Ne laser was used to conduct the tests at 25C.

PHASE ANALYSIS

A conductometer is used to measure the electrical conductivity of a nanoemulsion to determine its phase analysis.

ANALYSIS OF PARTICLE SIZE

The particle size of nanoemulsions is measured with a photon correlation spectrometer. At 25°C, a light scatter monitor at a 90° angle.

pH

A pH meter was used to measure the apparent pH of the formulation.

REFRACTIVE INDEX

The ratio of the velocity c of an undulating sound or light in a reference medium to the phase velocity vp of the wave in the medium is called the refractive index, abbreviated as n. n = c/vp was calculated at 250.5°C using an Abbes-type refractometer.

STUDIES ON IN VITRO SKIN PERMEATION

Keshary-Chien diffusion cells were used in in vitro skin permeation studies. It was performed using 12 diffusion cells, a circulating water bath, and abdominal skin from male rats weighing 25010 g. The donor and recipient chambers of the vertical diffusion cells were separated by the skins. Freshwater containing 20% ethanol was poured into the receiving chambers. The solution in the wells was constantly stirred at 300 rpm while the wells were heated to a temperature of 37º C. The dispensing chamber was filled with the compositions. After 2, 4, 6, and 8 hours, 0.5 mL of the solution was removed from the receiving chamber for analysis and immediately topped up with an equal volume of brand-new solution. In each case, the same sample was used three times. Cumulative adjustments were made to determine the total amount of drugs dispensed in each time interval. Graphs were generated as a function of time showing the total amounts of drugs that passed through the skin of rats. The slope of the linear portion of the cumulative amount permeated through rat skins per unit area versus time was used to calculate steady-state drug permeation rates across rat skins.

STUDIES OF THERMODYNAMIC STABILITY

The thermodynamic stability of drug-loaded nanoemulsions is reported after stress tests. Heating and Cooling Cycle: Nanoemulsion compositions underwent six cycles with cooling temperatures ranging from 4°C to 45°C. The centrifugation test was then performed on the stable formulations.

CENTRIFUGATION

The nano emulsion formulations that showed no phase separation after centrifugation at 3500 rpm were selected for the freeze-thaw test.

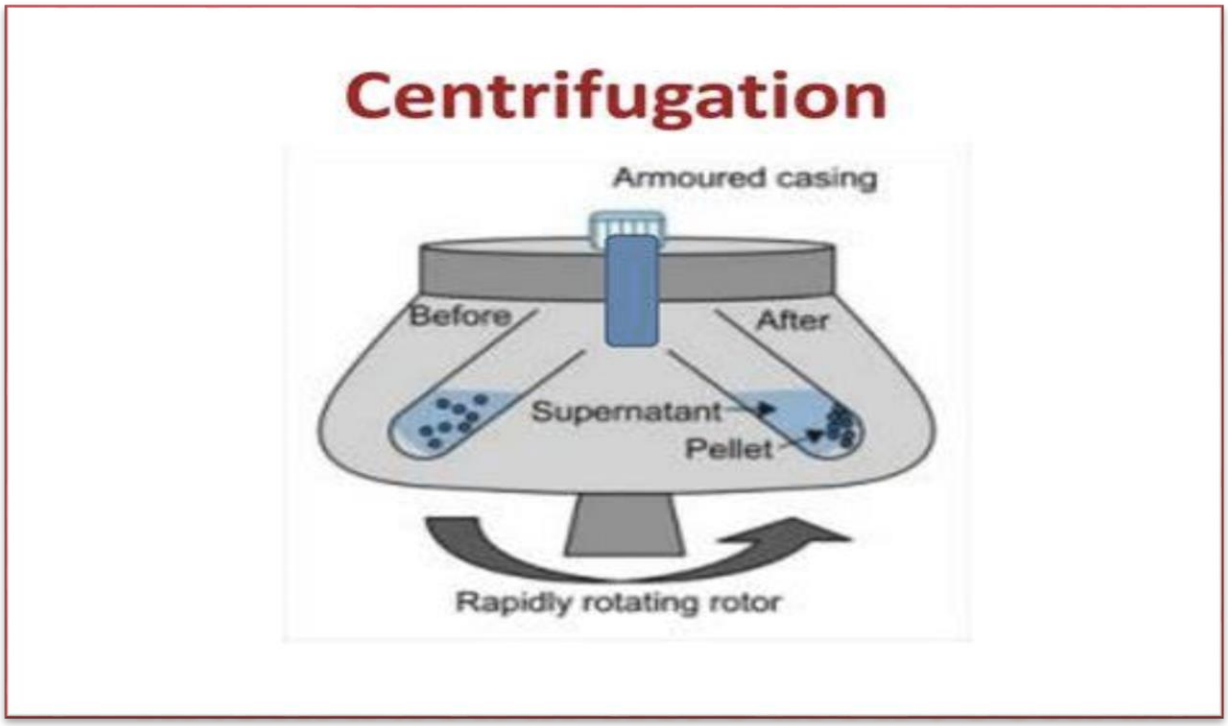

FIG: CENTRIFUGATION

FREEZE-THAW CYCLE

Three freeze-thaw cycles between 21°C and +25°C, maintained under standard laboratory conditions, were performed on the formulation in this experiment. Three months were spent on these studies. The ratio of the velocity c of a sound or light wave in a reference medium to the phase velocity vp of the wave in the medium is known as the refractive index, abbreviated as n. n = c/vp was calculated at 250.5°C using an Abbes-type refractometer.

USES FOR NANOEMULSIONS

COSMETICS THAT USE NANOEMULSIONS

The use of NEs as potential carriers for the regulated delivery of cosmetics and the optimal distribution of active ingredients in specific skin layers has recently gained importance. Because of their internal lipophilicity, NEs are

preferable to liposomes for the delivery of lipophilic substances. They support the penetration of active ingredients into the skin and thus increase their concentration in the skin, similar to liposomes. Another advantage is the large surface area of the small droplet, which allows the active ingredient to be efficiently delivered to the skin. In addition, NEs are becoming increasingly popular due to their inherent bioactive effects. This can reduce transepidermal water loss (TEWL) and strengthen the skin's barrier function. NE is suitable.

NANOEMULSIONS IN THE SCIENCE OF CELL CULTURE

Cell cultures are used for in vitro testing or to produce biological substances such as recombinant proteins or antibodies. Blood serum or several certain compounds can be added to the culture medium to enhance cell development. Only small amounts of these lipophilic compounds could be taken up by the cells, making it very difficult to replenish the media with oil-soluble molecules accessible to the cells. A novel technique for delivering oil-soluble materials to mammalian cell culture is the use of NEs. Based on a NE stabilized by phospholipids, the method of administration. These translucent NE filters of 0.1 mm can be passed through for sterilization. The NE droplets. The cells rapidly absorb NE droplets. Therefore, the encapsulated oil-soluble compounds have high bioavailability for cells in culture. Better uptake of oil-soluble supplements in cell cultures, improved growth and viability of cultured cells, and acceptability of toxicity studies of oil-soluble drugs in cell cultures are all advantages of using NEs in cell culture technology.

PARENTERAL INFUSION

Due to the stringent requirements of this route of administration, particularly the requirement for the formulation droplet size to be less than 1 micron, the nanoemulsion has advantages for intravenous administration. Nanoemulsions are administered parenterally (or intravenously) for several reasons, including nutritional (e.g., fats, carbohydrates, vitamins, etc.). When administered parenterally, nanoemulsion formulations have distinct advantages over macroemulsion systems because the small particles in nanoemulsions clear more slowly than in coarse emulsions, giving them a longer residence time in the body. O/W and W/O nanoemulsions can be used for intravenous administration.

ORAL PRESENTATION

For oral administration, nanoemulsion formulations offer several advantages over traditional oral formulations, such as B. Improved clinical efficacy, increased absorption, and reduced drug toxicity. The nanoemulsion thus demonstrates delivery, including better clinical efficacy, greater absorption, and reduced drug toxicity. As a result, Nanoemulsion is effective in administering drugs such as steroids, hormones, diuretics, and antibiotics. Pharmaceutical drugs made from proteins and peptides are extremely effective and target specific physiological processes. Primaquine demonstrated potent antimalarial activity against Plasmodium bergheii infection in mice when contained in an oral lipid nanoemulsion at a 25% lower dose compared to a standard oral dose. Primaquine lipid nanoemulsion increased oral bioavailability through the liver by at least 45% higher drug concentrations than neat drugs.

TOPICAL DELIVERY

Avoiding first-pass hepatic metabolism of the drug and its associated adverse consequences is one of the advantages of topical drug delivery over other approaches. Another reason is the drug's ability to spread directly to the affected skin or eyes. Only systemic antibiotics could achieve the high level of topical antibacterial activity that the nano emulsion is capable of. The nano emulsion shows a broad spectrum of activity against fungi and bacteria, including S. aureus, Candida, and E. coli.

DELIVERY TO THE EYES

The majority of drug delivery for the treatment of eye diseases is topically. To increase absorption, achieve a prolonged release profile, and dissolve poorly soluble drugs, nanoemulsions have been investigated for ocular administration.

TRANSCUTANEOUS

The anti-inflammatory effects of a truly optimized nanoemulsion formulation and a labeled gel in carrageenan-induced paw edema in rats were compared using the potent NSAID indomethacin. There is great potential for the transdermal application of indomethacin as the percentage inhibition for the prepared nanoemulsion was significant. Celecoxib was delivered transdermally using nanoemulsions of 2% celecoxib, 10% oil phase (Sefsol 218 and Triacetin), 50% surfactant blend (Tween 80 and Transcutol-P), and 40% water. Celecoxib gel (43.7%) and nanoemulsion gel (64.5%) were shown to have lower anti-inflammatory activity and percent inhibition than the nanoemulsion formulation (81.2%). The in vitro in vivo studies showed that the aceclofenac nanoemulsion had much more potent anti-inflammatory effects (82.2%) than conventional gels (71.4%) and nanoemulsion gel formulations.

NANOEMULSIONS IN CANCER THERAPY

Nanoemulsions can be used as vehicles in cancer chemotherapy to prolong the drug release rate after intramuscular and intratumoral injection (w/o systems). It also enhances transdermal drug delivery due to an increase in the transport of anticancer drugs via lymphatic permeation through the skin and it is also a non-irritating system.

ANTIMICROBIAL NANOEMULSIONS

Antimicrobial NEs are oil-in-water droplets in the range of 200 to 600 nm. They consist of oil and water and are stabilized by surfactants and alcohol. The NE has a broad spectrum of activity against bacteria (e.g. E. Coil, Salmonella, S. aureus), enveloped viruses (e.g. HIV, Herpes simplex), fungi (e.g. dermatophytes and candida), and spores (e.g .anthrax).

Thermodynamic forces force the NE particles to fuse with lipid-containing organisms. The anionic charge of the pathogen and the cationic charge of the emulsion are electrostatically attracted to each other, facilitating this

merging. Part of the energy contained in the emulsion is released when enough nanoparticles combine with the pathogens. The lipid membrane of the pathogen becomes unstable due to the active substance and the resulting energy, which leads to cell lysis and cell death. If spores form, additional germination enhancers are added to the emulsion. The germinating spores become susceptible to the antibacterial action of the NE once germination has begun. The NEs have a special property in that they selectively poison microorganisms in non-irritating concentrations.

SUMMARY AND CONCLUSION When it comes to distributing pharmaceuticals, biologics, or diagnostics, non-ferrous formulations offer several advantages. Traditionally, NEs have been used as total parenteral nutritional fluids in clinics for more than 40 years. Other drug delivery items have also entered the market including Diprivan, Liple, and Ropion. Although NEs are mainly used as delivery systems for water-insoluble drugs, colloidal carriers for the targeted delivery of certain anticancer drugs, photosensitizers, neutron capture therapy agents, or diagnostic agents have recently attracted considerable attention. Because of their submicron size, they can easily target the tumor site. In addition, the potential for surface functionalization with a targeting moiety has created new opportunities for the targeted delivery of drugs, genes, photosensitizers, and other substances.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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