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Review On Nanoemulsion

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ABSTRACT:

Nanoemulsions are kinetically stable liquid-in-liquid dispersions with droplet sizes typically around 100 nm. Due to their small size, they have special properties such as high surface area per unit volume, high stability and high visibility. These properties make nanoemulsions very versatile and find applications in many areas such as drug delivery, food, cosmetics, medicine and information science. Preparation of nanoemulsions can be done using high and low energy such as high-pressure homogenization, ultrasonic treatment, phase change temperature and emulsion inversion point technology. Recent developments have introduced new techniques such as foaming techniques to further improve the process.

***Keywords*:** Nanoemulsion, Homogenization, Emulsification, Characterization.

INTRODUCTION:

Nanoemulsions are thermodynamically stable colloidal dispersion frameworks consisting of two immiscible liquids mixed with emulsifiers (surfactants and co-surfactants) to form a phase. Nanoemulsions contain oil, water and emulsifiers. The swelling of the emulsifier forms the basis of nanoscale beads because it reduces the interface or surface energy of a region between the oil and water phases in the emulsion. Emulsifiers are essential for ensuring the stability and functionality of nanoemulsions, primarily through electrostatic repulsion and steric hindrance mechanisms. These mechanisms help prevent droplets within a nanoemulsion from merging, which is crucial for maintaining a stable dispersion and a consistent droplet size over time. However, over the years, emulsifiers have begun to be used as surfactants in the preparation of nanoemulsions. Research focuses on the preparation of nanoemulsions by various techniques and is broadly divided into two groups as high-tech and low-tech. High-pressure methods such as high-pressure homogenization (HPH) and ultrasound However, low-energy techniques violate the good principle of forming small droplets that do not absorb significant amount of energy (~103 W/kg). Both the Phase Inversion Temperature (PIT) and Emulsion Inversion Point (EIP) techniques are efficient, low-energy methods for producing nanoemulsions. These approaches leverage changes in thermodynamic properties and composition, instead of applying high shear forces, to generate nano-sized droplets. Recently, some new aq advances have been made in the fabrication of nanoemulsions, such as bubble spraying and evaporative aging at the oil/water interface. Here, we present different techniques for the fabrication of nanoemulsions and discuss methods to control and predict particle size based on their basic operating properties and methods. Nanoemulsions are kinetically stable, meaning that

given enough time, nanoemulsion-emulsion phase separation occurs. [1] . The nanoemulsion, which enters the aqueous phase with pressure extrusion technology, is made of surfactants approved for human consumption and is produced with "generally recognized" food products FDA certified safety (GRAS). This ointment is easily produced in large quantities by mixing water-immiscible oils from around the world [2].

Advantages of Nanoemulsions: [3,4]

- Reduces contrast absorption
- Makes the liquid more lipophilic
- Used to mask odors
- Used in the delivery of drugs via various routes such as blood transfusion, oral, And cosmetics.
- Effective and rapid penetration of the drug into the skin and gastrointestinal tract.
- Nanoemulsions have higher surface area and free energy than macroemulsions, making them more transportable.
- Nanoemulsions do not have the emulsification, agglomeration, coalescence and sedimentation problems that are usually associated with coarse emulsions.
- Nanoemulsions can be converted into various formulations such as foam, cream, liquid and spray.
- Nanoemulsions are non-toxic and non-irritating and therefore can be used safely on the skin and mucosa.
- Nanoemulsions do not harm human health and animal brains and are therefore suitable for human and veterinary therapeutic purposes.

Disadvantages of Nano-emulsions: [5]

- Surfactants and co-surfactants important for stability must be used in large quantities.
- The stability of nanoemulsions is affected by environmental factors such as pH and temperature.
- Materials with high melting points have low dissolution ability.

Limitations of Nanoemulsions: [6]

Although this formulation has advantages in terms of delivery to the customer, sometimes the reduction of water content results in the use of less nanoemulsion. Some limitations of nanoemulsions are as follows :

- The production of nanoemulsion formulations tends to be expensive, largely due to the difficulty in achieving the targeted droplet size. This process requires specialized equipment and advanced processing techniques to create the extremely fine droplets characteristic of nanoemulsions. For example, the homogenizer configuration (an equipment required for nanoemulsion formulation) is an expensive process to set up. Similarly, microfluidization and sonication (production techniques) also need a lot of financial support.
- This issue has posed a considerable challenge for an extended period.. Ostwald ripening is the main factor associated with the formation of unstable nanoemulsions. This is because the high curvature of small droplets indicates greater solubility compared to larger droplets with smaller radius of curvature.
- Less surfactant and co-surfactant required to make nanoemulsions is another factor limiting the production of nanoemulsions.

Types of Nanoemulsions: [7,8]

According to the difference between the oil phase and the water phase of the nanoemulsion, it is divided into three types:

- **oil-in-water (o/w) nanoemulsion**, in this system the oil droplets of the internal phase are dispersed
- **water-in-oil (w/o) nanoemulsion**, in this system the water droplets in the internal phase are dispersed in the external oil phase.
- **Bi-continuous Nanoemulsion** Small-sized bicontinuous nanoemulsions work by spatially distributing oil and water within the framework.
- **Water – in-oil-in-water (W/O/W).**
- **Oil-in-water-in-oil (O/W/O).**

The stability of the three types of nanoemulsions is achieved by adding sufficient amounts of surfactant and co-surfactant to reduce the interaction between anionic, cationic and nonionic surfactants.

Components of Nanoemulsions:

- Oil
- Surfactant
- Co- Surfactant
- Aqueous phase

Oil:

The selection of the oil used in nanoemulsion formulations is considered important because the drug will be placed in the oil phase as droplets dispersed in the aqueous phase. Therefore, the selected oil must be able to dissolve the drug in the dosage form to obtain more drug and the selected oil must be compatible with other nanoemulsion components. The oils used in nanoemulsions can be natural, synthetic or semi-synthetic.[9]

Surfactant (surface-active agent):

Surfactants are substances that reduce the interfacial tension or surface tension between solids and liquids.Surfactants can act as emulsifiers, wetting agents, foaming agents, detergents and dispersants depending on their hydrophilic-lipophilic (HLB) value. The purpose of surfactants in the preparation of nanoemulsions is to stabilize the system And are selected as the type of nanoemulsion to be prepared. Hydrophilic surfactants HLB value is higher > For 10 O /w nanoemulsions, hydrophobic surfactants with an HLB value below 10 are used for w/o nanoemulsions.The combined use of surfactants with low and high HLB values leads to the formation of nanoemulsions with good stability when diluted with water.[10]

Table(1). Surfactant property according to HLB value.[12]

HLB Value	Surfactant Property
(0-3)	Anti-foaming agent
(4-6)	Water in oil (O/W) emulsifiers
(7-9)	Wetting agent
(8-18)	Oil in water (O/W)emulsifiers
(13-15)	Detergents
(>15)	Solubilizing agent

Co- Surfactant:

While surfactants cannot reduce the interface between oil and water, adding these materials to nanoemulsion formulations can reduce the interface between oil and water. In addition, when the surfactant has high hardness, it can enter the monolayer of the surfactant, give a certain fluidity to the interfacial tension of the surfactant, and destroy its crystalline liquid phase, that is, Co – surfactants. [11]

Aqueous phase:

Deionized water was used as the aqueous phase in the nanoemulsion formulation because it has a pH of 7 and does not contain electrolytes. The stability of nanoemulsions and their small droplets is affected by the properties of the aqueous phase such as ion content, electrolytes, and pH. Electrolytes reduce the repulsive force of water droplets due to the decrease in zeta potential and change in pH structure, which causes the droplets in the formulation to agglomerate.[13]

Method Of Preparation Of Nanoemultion:

There are two main methods for preparing nanoemultions[14]:

Persuastion , Brute force

***Persuation*:**

Phase shift from near-optimum with a change in a variable: This method involves a change from near-optimum in a variable such as salinity or temperature (HLD (hydrophilicity)) to 0), for example use a higher temperature for the microemulsion.

Obtaining a step change from near-optimum with variable changes: This method involves multiple change maps, for example use a higher temperature and Add more salt to the microemulsion.

Catastrophic inversion: This method involves inversion of the lower inner emulsion, so that the inner phase becomes the outer phase.

Formation of stable phase transition from liquid crystal : This method has stable nanodroplets by forming liquid crystal from the state close to HLD = 0.

***By Brute force*:** This method is very open, using high-speed electrical equipment, high-pressure homogenizers, ultrasonic frequency equipment, small holes, etc. W/O nanoemulsions are very clear, and the formation of nanoemulsions by condensation or low-energy emulsification method takes advantage of the physical and chemical properties of the systems based on the phase changes that occur during the emulsification process.

It works by operating at very low interfacial tension in certain areas of the phase diagram, these are the liquid crystals and microemulsion areas; finally forming the Nanoemulsion of the emulsification process. The properties of nanoemulsions, such as small droplet size, relatively high kinetic stability and optical

transparency, are revealed not only by compositional variables, but also by preparation variables such as the emulsification method, the degree of mixing energy input and the emulsification time.

Techniques of preparation of nanoemultion:

High Energy Emulsification Method:

In this process, the droplet size of air emulsions is reduced with the help of ultrasonic devices.This machine can only produce small nanoemulsion particles, it includes Ultra-sonication, high pressure homogenization, microfluidization, high energy stirring and membrane emusification [15-21]

High-Pressure Homogenization:

This machine uses a high-pressure homogenizer / piston homogenizer to produce small-sized (up to 1 nm) nanoemulsions. In the high-pressure homogenizer, the dispersion of two liquids (oil phase and water phase) is achieved by forcing their mixture through a small inlet port at high pressure (500 to 5000 psi), subjecting it to strong turbulence and hydraulic shearto form a very fine emulsion.Different types of homogenizers are available for the production of nanoemulsions on a laboratory scale and industrial scale.This device works very well,The only drawback is the high density,The temperature of the emulsion increases during processing[22].

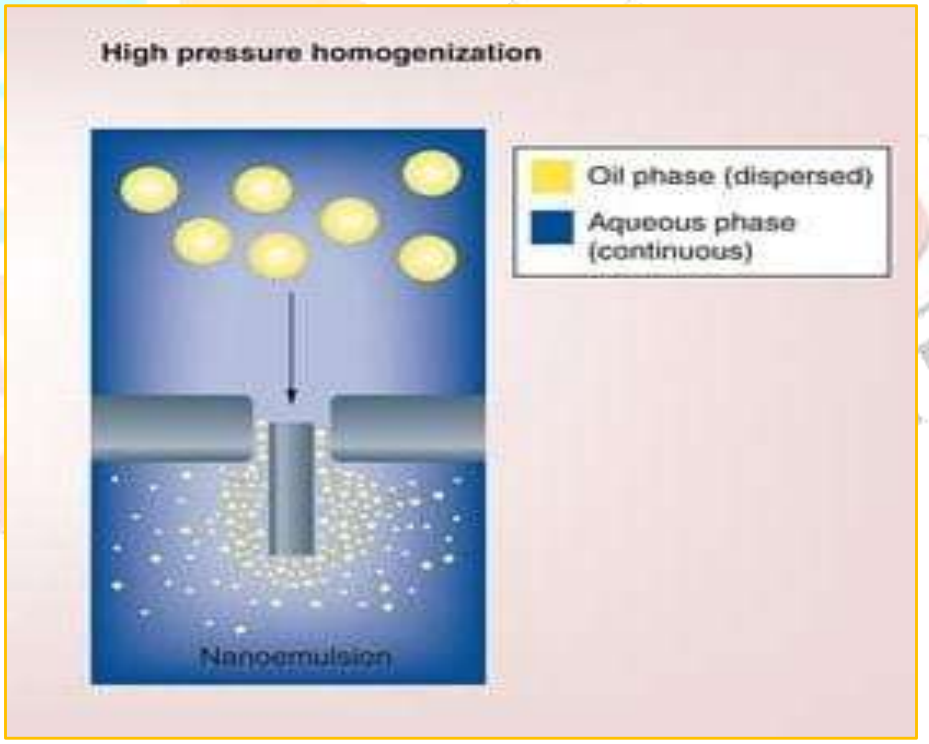

Fig.(1). Schematic controller mechanism of high pressure and homogenization reactor

Ultrasonic emulsification:

Ultrasonic emulsification is effective in reducing small amounts. In phacoemulsification, the energy is provided by an ultrasound machine called an ultrasound probe. It has a piezoelectric quartz crystal that expands and contracts in response to AC voltage. When the tip of the ultrasonic generator comes into contact with the liquid, all kinds of vibrations are created and cavitation occurs. Cavitation is the formation and collapse of vapour cavities in liquids. Therefore, ultrasound can be used directly to form emulsions; It is typically used in laboratories where emulsion droplet sizes are as small as 0.2 microns.[15-21]

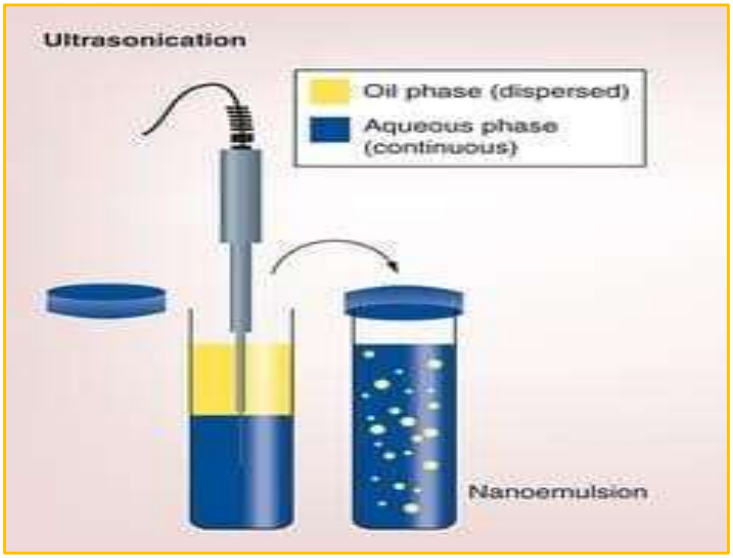

Fig.(2). The reaction of ultrasonication approach.

Microfluidization Mechanism:

Microfluidization is a patented mixing technology that uses a device called a microfluidizer. The device uses a high-pressure pump (500-20,000 psi) to force material through an interaction chamber made up of tiny channels called "microchannels." The particles flow into the affected area from the microchannels and form very fine submicron particles. The two solutions (aqueous and oil phases) are combined and processed in a homogenizer line to form a coarse emulsion. The crude emulsion enters the microfluidizer where it is further processed to obtain stable nanoemulsions. The coarse emulsion is passed through the interaction microfluidizer several times until the desired size is reached. The bulk emulsion was then filtered through a filter under nitrogen to remove large droplets, thus forming a mixed nanoemulsion. Another method used in nanoemulsion preparation is phase change technology.[23-26]

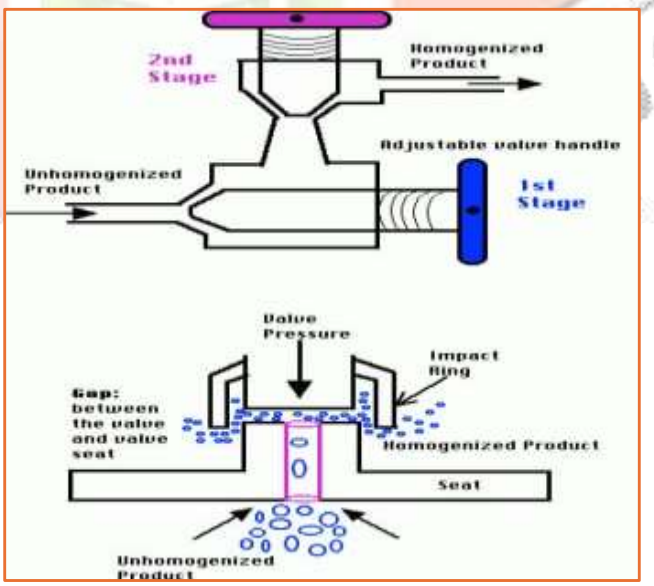

Fig.(3). Reaction mechanism of microfluidizer.

Low energy emulsification method:

Phase Inversion Temperature Method:

Fine scattering is achieved by the material dynamics created by the phase changes occurring in emulsification technology. A sufficient phase is achieved by changing the composition at a constant temperature or by changing the temperature of the composition. Based on the principle that the solubility of polyoxyethylene surfactant changes with temperature, a phase inversion temperature (PIT) strategy was proposed. As the temperature increases, the surfactant becomes lipophilic due to dehydration of the polymer chain. At low temperatures, the surfactant monolayer has a positive curvature and forms a micellar solution phase that swells in oil.[27]

Solvent Displacement Method:

Solvent evaporation emulsions are always creative and there are two main methods used for emulsion development; preparation of one emulsion such as oil in water (o/w) or two emulsions such as (water in oil) in water - water, (water/water)/water. This technique uses evaporation of the solvent by high speed homogenization or sonication followed by continuous magnetic stirring at room temperature or under low pressure. After a short time, the mixed nanoparticles can be collected by ultracentrifugation and washed with distilled water to remove additional substances such as surfactants.[28]

Phase Inversion Composition Method:

Phase inversion of microemulsions refers to the transition from O/W to W/O systems when non-ionic surfactants are used to change the product phase, for example by incorporating a rich dispersed phase or by temperature. The arched structure allows the framework to be stretched to an incredible level and forms a good fuel. This method allows a large change in molecular size, which contributes to the change in drug release patterns in vivo and in vitro.[29]

Characterization of nanoemulsions

Nanoemulsions are thermodynamically unstable and therefore their properties depend on the preparation method. Here we discuss some parameters that need to be analyzed when preparing nanoemulsions[30].

Phase behaviour study:

This study is the characterization and optimization of the product (surfactant, oil phase and aqueous phase). In general, research is needed to determine the phase and dispersion of nanoemulsion for nanoemulsion formulations prepared by phase inversion heat method and self-emulsification method. The research is to put nanoemulsions of different products into glass ampoules change the concentration and homogenize them thoroughly at one temperature at a time until they reach equilibrium. Anisotropic phases can be identified by polarized light

Particle Size Analysis:

It is essential to evaluate the hydrodynamic particle size and particle size distribution of formulated nanoemulsions. Dynamic light scattering (DLS) is usually used for the measurement of particles and additional particle size distribution in nanoemulsions.

Surface charge measurement:

The zeta potential of nanoemulsion droplets should be measured with the help of microelectrodes to estimate the surface properties of nanoemulsions.

Transmission Electron Microscopy (TEM):

This method is used to analyze the morphology of nanoemulsions.

Drug Contain:

This method is used to determine the drug content in the preparation. Many methods (especially the Western Blot method) are used in this determination.

Viscosity:

Viscosity must be measured to ensure formula quality.

Nanoeulsion instability and its prevention methods:

The instability of nanoemulsions is caused by some important factors, including emulsification [31], flocculation [32, 33], coalescence [34] and Ostwald ripening [35]. Among them, Ostwald ripening is the main mechanism of nanoemulsion instability, because the residual problems can be reduced by the small size of nanoemulsions and the use of nonionic surfactants. The rapid movement of small droplets prevents the emulsification of nanoemulsions. Van der Wall forces are responsible for attracting water droplets and causing emulsion agglomeration. However, nanoemulsion does not create an attraction for nonionic surfactants, so agglomeration does not occur. Small droplets of nanoemulsions also prevent agglomeration because these small droplets expand the curvature pressure, while Laplace pressure resists the deformation of large droplets [36]. To prevent this, a thick, multilayered surfactant film is used at the interface [37].

The only instability problem in nanoemulsions can be caused by Ostwald ripening. In Ostwald ripening, small droplets with high radius of curvature transform into large droplets with low radius of curvature loss [38] Therefore, after long-term storage, the droplet size distribution changes to a larger size and the transparency of nanoemulsion becomes cloudy. Ostwald ripening is also found to be a problem during the distribution of formulations. Many theories have been put forward to justify the development of Ostwald; among them, the theory of LSW is to show the characteristics that affect the development of Ostwald. Tadros et al. showed that the addition of a small amount of insoluble oil (squalene) reduced the diffusion of small oil from small to large oil. Another way to prevent the Ostwald ripening effect is to add polymeric surfactants to the interface, which increases the elasticity of water droplets and further reduces the Ostwald ripening effect [39].

Paqui Izquier et al. obtained the effect of surfactant mixture on the stability of nanoemulsions while using phase inversion as a preparation method for nanoemulsions. The formation of O/W nanoemulsions was studied using the PIT emulsification method in water/mixed nonionic surfactant/oil system. The combination of polyoxyethylene 4-lauryl ether (C12E14) and polyoxyethylene 6-lauryl ether (C12E6) can change the hydrophilic and lipophilic properties of the surfactant. Emulsification was carried out by rapidly cooling from the corresponding HLB temperature to 25 °C in normal oil sample (20 wt%). When the total surfactant concentration was 4 wt% and 8 wt%, nanoemulsions with drop radii of 60-70 nm and 25-30 nm were obtained. Nanoemulsions with 8 percent surfactant content showed greater stability than nanoemulsions with 4 percent surfactant concentration [40]. In another study, Sher L. et al. obtained the effect of different methods on nanoemulsion droplet size, which contributes to the stability of nanoemulsions. In their study, they investigated the formation and stability of n-decane in aqueous nanoemulsions produced by PIT method using polyoxyethylene lauryl ether as surfactant. The results of this study clearly show that the small droplets of nanoemulsions depend on many different processes such as heating and cooling of the sample and the final temperature at which the mixture is cooled after phase inversion [41].

In another study, The effect of surfactant and surfactant concentration on the disintegration and coalescence process in high-pressure homogeneous aqueous nanoemulsions was investigated. All formulations were studied at different concentrations and sizes using protein, phosphatidylglycerol and phosphatidylcholine as surfactants. It was found that for proteins, the volume increased linearly with time, indicating the Ostwald ripening process. Although there was synergistic protection at the lowest phospholipid concentration used, ripening was not observed at any emulsifier concentration, suggesting that the structure of the phospholipid-phospholipid interface is a mechanism preventing ripening [42]. Porras M [43] showed that the combination of surfactants increased stability compared to single surfactants. It has also been shown that the stability of electrostatically and sterically stabilized dispersions can be controlled by the value of the electric double layer and the thickness of the unformed droplet layer[44].

Application of Nanoemulsions in cosmetics:

Nanoemulsions have recently become more important as potential carriers for controlled delivery of cosmetics and optimization of distribution of active ingredients in the skin system. Due to their inherent lipophilicity, nanoemulsions are better than liposomes in transporting lipophilic compounds. Nanoemulsions are accepted in cosmetics because there is no inherent emulsification, solution, aggregation or coalescence in macroemulsions. The use of high voltage equipment during the manufacturing process often prevents the integration of potential ingredients into a crucible [45].

In recent years, nanoemulsions have attracted great attention due to their applications in personal care products, as they can control cosmetics and, in particular, optimize the distribution of active ingredients in the skin[46].

Antimicrobial Nanoemultion:

Antimicrobial nanoemulsions are oil-in-water droplets ranging from 200 to 600 nm. They are made of oil and water stabilized with surfactants and alcohol. They protect against bacteria (such as E. coli, salmonella, Staphylococcus aureus), bacterial infections (such as HIV, herpes simplex), fungi (such as Candida, dermatophytes), and spores (such as anthrax). Nanoemulsion particles are thermodynamically driven to fuse with lipid-containing organisms.

This fusion is powered by the electrostatic attraction of the cationic charge of the emulsion and the anionic charge of the bacteria. When a sufficient number of nanoparticles combine with the bacteria, they release some energy into the emulsion. Both the active ingredients and the energy released destabilize the bacterial lipid membrane, causing cell lysis and death. Add germination promoters to the emulsion for spores. When germination occurs, the germinated spores are exposed to the antimicrobial agent of the nanoemulsion. Therefore, nanoemulsions can achieve the level of local antimicrobial activity previously achieved by topical antibiotics [47,48].

As A Mucosal Vaccine:

Nanoemulsions are used to deliver more protein or inactive bacteria to mucosal cells to produce antibodies. The first application, a vaccine against influenza and HIV, may enter clinical trials. Nanoemulsions allow proteins coated on the mucosal surface to act as adjuvants and support the immune system. Additional studies are ongoing to complete proof of concept testing in animals for other vaccines, including hepatitis B and anthrax [49]. In mice, the combination therapy elicited positive anti-gp120 IgG as well as bronchial, genital, and anti-gp120 IgA antibodies.

Fluids from these animals exhibited antibodies associated with the heterologous gp120 serotype and were neutral to two types of HIV B (HIVBaL and HIVSF162) and five major and operant. Analysis of gp120-

specific CTL proliferation, INF-g induction, and the prevalence of antigp120 IgG2 subclass antibodies showed that nasal vaccination with nanoemulsions also induced a systemic Th1-polarized cellular immune response. This study suggests that nanoemulsions should be evaluated as mucosal adjuvants for multivalent anti-HIV drugs [50]. Despite the availability of safe and effective vaccines, hepatitis B infection remains a major public health problem worldwide. Limitations of these vaccines include the need for refrigeration and the three-dose requirement, which precludes their use in developing countries. A new hepatitis B vaccine made from hepatitis B antigens (HBsAg) and a novel nanoemulsion adjuvant (HBsAg-nanoemulsion) requires a lower dose to be effective. Excellent toxicology tests proved that the HBsAg nanoemulsion vaccine is safe and effective in various animal species. Our results suggest that non-injection administration of HBsAg-NE may be an anti-hepatitis B drug or another anti-viral drug for parenteral hepatitis B. This vaccine induces Th1-mediated cell protection and may also provide therapeutic benefits for: Chronic hepatitis B patients who lack an immune system to control the infection in their body. The long-term stability of this reaction at high temperatures suggests a good trend in this area, as the potential difference in maintaining cold chains can be prevented without good clinical consequences [51].

A new technique for injecting multiple vaccines – using an oil-based emulsion inserted into the nose instead of a needle – has been shown to produce antibodies that block the small virus. Two HIV products in new research. Improving mucosal immunity is also important in preventing HIV. Studies have shown that an anti-HIV nanoemulsion drug can boost the immune system, prevent cell infection and prevent several types of HIV infection. The protein used by the group, gp120, is one of the most important proteins studied in other HIV drugs [52].

Nanoemulsion as Non-Toxic Disinfectant Cleaner:

EnviroSystems, Inc. has developed non-toxic disinfectants for use in industries such as healthcare, hospitality, travel, food processing, and military applications. Tuberculosis is deadly and contagious. This item does not require a notification. It is not irritating to the eyes and can be absorbed through the skin, inhaled, or swallowed. This disinfectant consists of #106 mm oil nanospheres suspended in water to produce NE containing only trace amounts of the active ingredient PCMX (p-chlorometa-xylenol). The nanospheres carry surface charges that can penetrate the surface of microbial cells like an electric fence. The formula does not "water" the cells but allows PCMX to target and penetrate the cell wall. Therefore, PCMX is 1-2 times less potent than other antibiotics, so it is not toxic to humans, animals or the environment. Other microbial antibiotics require large doses of ingredients to surround and destroy bacterial cells; the importance of soaking them in the antibiotic. The formula is a general disinfectant that can be used on all hard surfaces including appliances, cabinets, walls, fixtures and floors. A single product can now replace many, thus reducing inventory and saving valuable storage space[53,54].

Nanoemulsion in Cell Culture Technology:

Cell culture is used for in vitro analysis or production of biological substances such as antibodies or protein complexes. Various specific molecules or sugars can be added to the culture medium to enhance cell growth. The advantage of using nanoemulsions in cell culture technology is that lipid-soluble substances are better absorbed in cell culture, increasing the growth and success of the culture and allowing research on the toxicity of lipid-soluble chemicals [55,56].

The Role of Nanoemulsion in Cancer therapy and Targeted Drug Delivery:

The design and composition of nanoemulsion (Gd-nanoLE) on Gd biodistribution in gadolinium (Gd)-containing lipids D1-179 were evaluated. The use in neutron capture therapy for cancer after intravenous (IV) injection into melanoma-bearing hamsters. Biodistribution data show that Brij 700 and HCO-60 prolong the

retention time of Gd in the blood and improve its accumulation in tumors. After transdermal application, the drug is generally distributed into the deep layers of the skin with minimal leakage. The intrinsic bioavailability is 70.62%. D-TocopheroldzInhibition of P-glycoprotein efflux by polyethylene glycol 1000 succinate and labradorine increases the oral bioavailability of PCL This study provides direct evidence for the localization of high molecular weight lipophilic PCL in the dermis. Furthermore, nanoemulsion formulations increased oral bioavailability to over 70%. The established nanoemulsion formulation is safe and effective for both oral and dermal delivery of PCL [57].

Intranasal drug delivery:

The biggest obstacle to intranasal drug delivery targeting the brain is the existence of the blood-brain barrier (BBB). It prevents the entry of hydrophilic and high molecular weight molecules such as peptides. However, the olfactory nerves located in the nasal mucosa provide direct communication between the nose and the brain. This is done using nanoemulsions loaded with anti-Alzheimer's disease, anti-Parkinson's disease and brain-targeting antipsychotic drugs. Risperidone is an antipsychotic drug with low bioavailability due to first-pass metabolism. To reach the brain efficiently and avoid unnecessary side effects, techniques involving nanoemulsions that increase bioavailability by preventing first-pass metabolism and promoting blood-brain barrier transport are used. O/W nanoemulsions were produced by separating ris-piperidone in capmul MCM, Tween 80, transcutol and propylene glycol (48%, w/w). The ultrafine sphere size (15.5–16.7 nm) of the nanoemulsion produced enables rapid and efficient delivery of risperidone to the brain after intranasal administration [58]. Structure-based nanoemulsions are used as vehicles to present antigen (antibody) to dendritic cells infiltrating or underlying epithelial cells of the nasal mucosa. After enhancing intracellular uptake and processing, antigen-loaded nanoemulsions induced the migration of stimulated dendritic cells to regional lymph nodes within a day. The immune adjuvants were encapsulated in an O/W nanoemulsion (W805EC Nanoemulsion) that can be delivered intranasally as an adjunct to inactivated influenza vaccine. W805EC nanoemulsion adjuvant boosts the immune system and is better than parenteral injection[59].

Parenteral nanoemulsions:

Parenteral nanoemulsions have many applications. They are used to deliver drugs with low bioavailability and/or narrow therapeutic index. Chlorambucil is a lipophilic anticancer agent administered parenterally as a nanoemulsion (prepared using ultrasound and high-pressure homogenization) for the treatment of ovarian and breast cancer [60]. Tagne et al. developed a water-soluble tamoxifen nanoemulsion to increase its efficacy in the treatment of breast cancer [61,62]. TOCOSOL™ is a paclitaxel-containing vitamin E nanoemulsion produced by high homogenization and used in the treatment of various cancers such as ovarian cancer, breast cancer, etc. The efficacy of paclitaxel has been shown to be effective in preventing breast cancer, but unfortunately, the phase 3 trial did not reach the end. However, this does not affect the previous studies of TOCOSOL™, nor does it affect its production such as ultra-fine (40-80 nm), medium and stable. TOCOSOL™ produced better antitumor effects than the drugs used in the solution of colon adenocarcinoma model and therefore deserves further investigation [63]. In addition, our team also tried to slightly modify the paclitaxel-vitamin E nanoemulsion to improve the anti-inflammatory and anti-inflammatory activity of vitamin E. We found that drug-loaded nanoemulsions improved the immunogenicity of paclitaxel by opening alternative pathways for mitochondrial activation, pharmacokinetic enhancement, and immune modulation. Overall safety (as measured by blood markers and organ systems) was also improved [64]. Diclofenac O/W parenteral lipid nanoemulsion was investigated for the treatment of arthritis. Diclofenac nanoemulsions with an average size of 200 nm were prepared by high-pressure homogenization and ultrasonic treatment. Diclofenac nanoemulsions have been shown to provide inhibitory drug release in vivo and allow for significant dose reduction [65]. Nanoemulsions

can be converted into stealth/long-lived nanoemulsions by coating or adding hydrophilic moieties (such as PEG) to their surfaces, thus preventing their recognition by the mononuclear phagocyte system (MPS). Effects and consumption. For example, Haack et al. PEG-coated multifunctional nanoemulsions were successfully injected into the bloodstream [66]. They created nanodroplets using paramagnetic and fluorescent lipids (for multiplex detection and imaging) and then coated the nanodroplets with targeting ligands, RGD peptides and PEG. It is thought that the PEG layer will prevent MPS uptake, thus allowing the nanoemulsions to be attracted to the tumor microenvironment, while the RGD peptide will promote the recycling of droplets with Rvβ3 integrin present in the tumor microenvironment. To target diseases where bacteria are present in macrophages, such as tuberculosis and leishmaniasis, the MPS must be permeable, which is almost the exact opposite of the principle of invisible nanoemulsions. Kansal et al. developed a polyelectrolyte-coated nanoemulsion layer containing doxorubicin for the treatment of visceral leishmaniasis (caused by the bacteria in MPS). They used the phospholipid serine as a targeting ligand. This study found that phosphatidyl serine-coated nanoemulsions were significantly uptaken by macrophages, allowing the selective delivery of payloads deep into organs that are normally inaccessible in space[67].

Conclusion:

Nanoemulsions are widely used in medicine. The most important application of nanoemulsions is to mask the odor of oily liquids. Nanoemulsions can also protect chemicals that are subject to hydrolysis and oxidation. Today, nanoemulsions are used in the delivery of various antibiotics, antibiotics or therapeutic drugs. Nanoemulsions can also be used to extend the life of the drug. In general, the entire nanoemulsion formulation can be considered to be effective, safe and have strong bioavailability. It is expected that further research and development on nanoemulsions will be carried out in the future.

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