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A COMPREHENSIVE REVIEW ON NANOEMULSION: FORMULATION, CHARACTERIZATION, AND APPLICATIONS

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Abstract: A novel drug delivery system has been developed to address the limitations of conventional drug delivery methods. This comprehensive review explores the nanoemulsion system, which is designed to enhance the delivery of active pharmaceutical ingredients. Nanoemulsions are stable and homogeneous systems with nano-sized droplets formed by combining two immiscible liquids using surfactants and co-surfactants. The droplet size typically ranges from 10 to 500 nm, distinguishing nanoemulsions from traditional emulsions. This review provides insights into the formulation, preparation methods, characterization techniques, evaluation parameters, and diverse applications of nanoemulsion, offering a fundamental understanding of this innovative drug delivery system. diverse aspects of nanoemulsions, including excipients, manufacturing techniques, production conditions, structural dynamics, destabilization mechanisms, and drug delivery applications. By doing so, we hope to generate interest among those interested in exploring this field and provide valuable insights for their potential ventures.

Keywords*: Nanoemulsion, Oil, Surfactant, Cosurfactant, Ultrasonication, Biotechnology.*

Introduction:

Nanoemulsions are a type of emulsion where oil and water are dispersed using a suitable surfactant. They typically have a mean droplet diameter of around 500 nm, resulting in a clear or hazy appearance. This contrasts coarse emulsions with larger droplets, giving them a milky white color due to light scattering. While the terms nanoemulsion, submicron emulsion, and mini emulsion are sometimes used interchangeably, it's important to note that nanoemulsion should not be confused with microemulsion. Despite having a similar droplet size range as microemulsions, nanoemulsions differ significantly in their structure and long-term thermodynamic stability.[1]

Nanoemulsions can be formulated into various dosage forms, including liquids, creams, sprays, gels, aerosols, and foams. They can be administered through different routes, such as topical application, oral ingestion, intravenous injection, intranasal delivery, pulmonary inhalation, and ocular application. Compared to simple micellar dispersions, nanoemulsions have a higher capacity for solubilization and exhibit greater kinetic stability than coarse emulsions. They have found applications in industries like cosmetics and pesticides, serving as aqueous bases for delivering organic compounds.[2]

The small droplet size of nanoemulsions contributes to their long-term physical stability, preventing issues like creaming, sedimentation, and coalescence that commonly occur in larger emulsion droplets. The strong Brownian motion exhibited by the small droplets helps counteract gravity and viscosity-induced kinetic instability. In the case of parenteral administration, nanoemulsions have been used to solubilize and protect drugs from harsh environmental conditions, such as oxidation, pH changes, and hydrolysis. They can also be utilized to target specific organs by taking advantage of the enhanced permeability and retention effect or to evade the reticuloendothelial system.[3]

Type of nanoemulsion

There are various types of nanoemulsion systems distinguished by their composition and structure. The main categories of nanoemulsion systems include:

1. Oil-in-Water (O/W) nanoemulsion

In this system, the oil phase is dispersed as small droplets within a continuous aqueous phase. Surfactants or co-surfactants surround the oil droplets, resulting in a stable O/W nanoemulsion. O/W nanoemulsions find applications in pharmaceuticals, cosmetics, and food industries.[4]

2. Water-in-Oil (W/O) nanoemulsion

W/O nanoemulsions involve dispersing the water phase as small droplets within a continuous oil phase. Surfactants or co-surfactants encase the water droplets, providing stability to the W/O nanoemulsion. W/O nanoemulsions are commonly used in cosmetic and pharmaceutical formulations. [5]

3. Bi-continuous nanoemulsion

Bi-continuous or multiple emulsion systems contain interconnected continuous networks of both oil and water phases. Surfactants or co-surfactants stabilize the bi-continuous nanoemulsion. This type of system finds applications in pharmaceuticals and controlled drug delivery.[6]

4. Pickering nanoemulsion:

Pickering nanoemulsions rely on solid particles adsorbed at the oil-water interface for stabilization. These particles act as emulsion stabilizers, preventing droplet coalescence. Pickering nanoemulsions have gained attention due to their potential for natural and biocompatible stabilization.[7]

5. Microemulsion

Microemulsions are thermodynamically stable, transparent systems consisting of oil, water, surfactants, and co-surfactants. Droplets in microemulsions are typically smaller than those in nanoemulsions, ranging from a few nanometers to tens of nanometers. Microemulsions possess excellent solubilization capabilities and find wide usage in drug delivery and enhanced oil recovery.[8]

Composition of nanoemulsion:

Nanoemulsions consist of two primary components: an oil phase and an aqueous phase, along with surfactants or co-surfactants that act as stabilizers. The composition of a nanoemulsion can vary based on the specific application and desired properties.

1. Oil Phase

The oil phase typically comprises hydrophobic liquids, either single oils or a combination of different hydrophobic liquids. Examples include natural oils like vegetable oils, mineral oils, essential oils, or synthetic oils. The selection of the oil phase depends on factors such as the solubility of active ingredients, desired properties (e.g., viscosity, stability), and the intended application.[9]

2. Aqueous Phase

The aqueous phase consists of water or a water-based solution. It serves as the medium for dispersing the oil phase and other water-soluble components. The aqueous phase may also include additional water-soluble active ingredients, salts, or other components based on the specific formulation requirements.[10]

3. Surfactants

Surfactants play a vital role in stabilizing the nanoemulsion by reducing the interfacial tension between the oil and water phases. Typically, surfactants are amphiphilic molecules with both hydrophilic and hydrophobic regions. They can be classified as primary surfactants or emulsifiers, which help stabilize the droplets by forming a protective layer around them. Additionally, secondary surfactants or co-surfactants are often used in combination with primary surfactants to further enhance stability and improve formulation characteristics.[11]

4. Co-surfactants

Co-surfactants are optional components utilized in some nanoemulsion formulations to optimize stability and properties such as droplet size, viscosity, and texture. Co-surfactants can enhance the solubility of lipophilic components, improve the emulsification ability of surfactants, and contribute to the overall stability of the nanoemulsion system.[12]

5. Preservatives, antioxidants, and chemoprotectants

Preservatives used in nanoemulsion need to fulfill certain requirements, including low toxicity, heat and storage stability, compatibility with the formulation, affordability, easy availability, pleasant Odor, taste, and color, as well as possessing a wide antimicrobial spectrum. It is important to consider that microorganisms can survive in both the oil and water phases of the nanoemulsion, so the chosen preservative must be able to reach effective concentrations in both phases.[13]

Advantages of nanoemulsion:

Nanoemulsions provide numerous benefits compared to conventional emulsions and other delivery systems, positioning them as a favored choice across various industries.

1. Improved drug solubility: Nanoemulsions enhance the solubility of hydrophobic drugs, improving their formulation and delivery.
2. Increased drug bioavailability: The small droplet size of nanoemulsions increases the surface area available for drug absorption, leading to enhanced bioavailability.
3. Targeted drug delivery: Nanoemulsions can be designed to target specific sites or tissues in the body, allowing for precise drug delivery and reduced systemic side effects.
4. Enhanced stability: Nanoemulsions exhibit improved physical stability compared to conventional emulsions, leading to longer shelf life and better product quality.
5. Improved permeation through biological barriers: Nanoemulsions can overcome biological barriers, such as the skin or mucosal membranes, to enhance drug permeation and absorption.
6. Controlled drug release: Nanoemulsions can be formulated to provide controlled and sustained release of drugs, ensuring a consistent therapeutic effect.
7. Versatile formulation options: Nanoemulsions can accommodate a wide range of drugs, including hydrophobic and hydrophilic compounds, offering versatility in formulation design.
8. Improved sensory characteristics: Nanoemulsions provide desirable sensory attributes, such as a non-greasy texture and transparency, making them suitable for cosmetic and personal care applications.
9. Protection of active ingredients: Nanoemulsion formulations can protect active ingredients from degradation, oxidation, or interactions with external factors, such as light or heat.
10. Environmentally friendly: Nanoemulsions often require lower amounts of surfactants and co-surfactants, reducing the potential environmental impact associated with their use.
11. Enhanced delivery of lipophilic compounds: Nanoemulsions improve the solubilization and delivery of lipophilic or poorly water-soluble compounds, expanding their applicability in various industries.
12. Potential for combination therapy: Nanoemulsions can be used to deliver multiple drugs or therapeutic agents simultaneously, allowing for combination therapy and synergistic effects.

Limitations of nanoemulsion:

1. Energy-intensive manufacturing process.
2. Limited long-term stability.
3. Sensitivity to environmental factors.
4. Complex formulation requirements.
5. Limited loading capacity for high concentrations of active ingredients.
6. Potential surfactant toxicity concerns.
7. Cost considerations for production and formulation.
8. Challenges in scaling up production.
9. Potential for drug interactions with nanoemulsion components.
10. Regulatory challenges and approval process.
11. Limited understanding of long-term safety implications.
12. Need for specialized equipment and expertise.

Formulation of Nanoemulsions:

The formulation of a nanoemulsion involves the combination of an active drug, additives, and an emulsifier. There are two main methods for preparing a nanoemulsion: high-energy emulsification and low-energy emulsification. The high-energy emulsification method utilizes techniques such as high-energy stirring, ultrasonic emulsification, high-pressure homogenization, microfluidization, and membrane emulsification. On the other hand, the low-energy emulsification method includes approaches like phase inversion temperature, emulsion inversion point, and spontaneous emulsification. By employing a combined method that incorporates both high-energy and low-energy emulsification, it becomes possible to create reverse nanoemulsions even in highly viscous systems.

Table1: Technique use for nanoemulsions.

Sr. no	Technique use for nanoemulsion
1	High-Pressure Homogenization
2	Microfluidization
3	Ultrasonication
4	Low Energy Emulsification
5	Spontaneous Emulsification
6	Solvent Evaporation Technique
7	Membrane Emulsification
8	Hydrogel method

A. High-Pressure Homogenization:

High-pressure homogenization is a method used to prepare nanoemulsions. A high-pressure homogenizer or piston homogenizer is employed in this technique to produce nanoemulsions with remarkably small particle sizes, reaching as low as 1nm. The process involves forcing a mixture of two liquids (oily phase and aqueous phase) through a small inlet orifice at very high pressure (ranging from 500 to 5000 psi). This intense pressure generates turbulence and hydraulic shear, resulting in the formation of extremely fine emulsion particles. The particles consist of a liquid, lipophilic core surrounded by a monomolecular layer of phospholipids that separate it from the surrounding aqueous phase. High-pressure homogenization is highly efficient, but it consumes a significant amount of energy and can cause an increase in the emulsion's temperature during processing.[14]

B. Microfluidization:

Microfluidization is a mixing technique that utilizes a microfluidizer device to achieve efficient and precise particle size reduction. The process involves the use of a high-pressure positive displacement pump, which generates pressures ranging from 500 to 20000 psi. The product, consisting of both the aqueous and oily phases, is introduced into the microfluidizer device, where it passes through a series of microchannels in an interaction chamber. At the impingement area, intense shearing forces result in the formation of extremely fine sub-micron particles. Initially, a coarse emulsion is produced by combining the aqueous and oily phase solutions in an inline homogenizer. This coarse emulsion is then subjected to microfluidization, where it undergoes multiple passes through the microfluidizer device until the desired particle size is achieved. To obtain a uniform nanoemulsion, the bulk emulsion is filtered under a nitrogen atmosphere to remove any remaining large droplets. This process ensures the production of a stable and homogenous nanoemulsion suitable for various applications.[15]

C. Ultrasonication

Ultrasonication is a commonly used technique in the preparation of nanoemulsions. It involves the application of high-frequency ultrasound waves to an emulsion, typically in the range of 20 to 100 kHz. Ultrasonication utilizes the phenomenon of acoustic cavitation, which refers to the formation, growth, and collapse of microscopic bubbles in a liquid subjected to ultrasound. In ultrasonication, the high-intensity ultrasound waves create alternating high-pressure and low-pressure cycles in the emulsion. In regions of low pressure, the liquid experiences negative pressure, causing the formation of small bubbles or voids. These bubbles grow rapidly during the low-pressure phase and then implode or collapse during the high-pressure phase. The collapse of these bubbles generates intense local energy, resulting in several physical effects, including microstreaming, shockwaves, and high shear

forces. These effects induce the disruption and breakup of larger droplets into smaller droplets, leading to the formation of a nanoemulsion with reduced droplet size.[16]

Probe sonication, also known as tip sonication or direct sonication, is a technique used in the preparation of nanoemulsions and other dispersed systems. It involves the use of an ultrasonic probe, also known as a sonicator or ultrasonicator, to apply high-frequency sound waves directly to the sample. In probe sonication, the ultrasonic probe is immersed directly into the liquid sample, typically contained in a suitable vessel such as a beaker or test tube. The probe generates high-frequency sound waves, usually in the range of 20 to 100 kHz, which propagate through the liquid. As the sound waves pass through the sample, they cause alternating high-pressure and low-pressure cycles, resulting in the formation and collapse of microscopic bubbles, a phenomenon known as acoustic cavitation. The collapse of these bubbles generates localized energy in the form of shockwaves, microstreaming, and high shear forces.[17]

D. Low Energy Emulsification

Low-energy emulsification is a technique used to prepare oil-in-water (o/w) nanoemulsions. It capitalizes on the physicochemical properties of these systems by taking advantage of the phase transition that occurs during the emulsification process.[18]

E. Spontaneous Emulsification

Spontaneous emulsification involves three main steps. First, a homogeneous organic solution consisting of oil and a lipophilic surfactant is prepared in a water-miscible solvent along with a hydrophilic surfactant. Next, the organic phase is injected into the aqueous phase while under magnetic stirring, resulting in the formation of an oil-in-water (o/w) emulsion. Finally, the water-miscible solvent is removed through evaporation under reduced pressure.[19]

F. Solvent Evaporation Technique

This technique involves preparing a solution of the drug and subsequently emulsifying it in a nonsolvent liquid. The evaporation of the solvent leads to the precipitation of the drug. By employing high shear forces using a high-speed stirrer, crystal growth, and particle aggregation can be controlled during this process.[20]

G. Membrane Emulsification

Membrane emulsification employs a porous membrane as a dispersion device. The emulsion is forced through the membrane pores, resulting in the formation of droplets of a smaller size. This technique offers control over droplet size by manipulating the membrane properties.[21]

H. Hydrogel method

The Hydrogel Method is a technique used for nanoemulsion preparation that is similar to the solvent evaporation method. The main difference between the two methods lies in the solvents used. In the Hydrogel Method, the drug solvent is miscible with the drug anti-solvent. This miscibility allows for the formation of a hydrogel matrix. In the Hydrogel Method, the drug and anti-solvent are mixed to form a hydrogel. The hydrogel acts as a template or matrix for the formation of the nanoemulsion. The drug is encapsulated within the hydrogel, and the nanoemulsion is formed by incorporating the hydrogel into an aqueous medium.[22]

Characterization of nanoemulsion:

1. Droplet size analysis particle size distribution

Dynamic Light Scattering (DLS), also known as photon correlation spectroscopy or quasi-elastic light scattering, is a technique used to rapidly determine the size distribution profile of small particles in suspensions or polymers in solution. By analyzing the intensity fluctuations in the scattered light from particles illuminated by a laser, DLS can calculate the particle size based on the Brownian motion, using the Stokes-Einstein equation. This method provides a quick and effective evaluation of the size and size stability of nanoemulsions during storage.[23]

2. Zeta potential

Zeta potential refers to the electrokinetic potential in colloidal systems. It represents the potential difference between the dispersion medium and the stationary fluid layer attached to the dispersed particle. In colloidal chemistry, a zeta potential value of ±30 mV is often considered as a threshold to differentiate between low-charged and highly-charged surfaces. The zeta potential value indicates the level of repulsion between similarly charged particles in the dispersion, thereby affecting colloidal stability. Higher zeta potentials (positive or negative) confer electrical stability and resist aggregation, while lower zeta potentials lead to attraction,

resulting in flocculation or coagulation. In summary, zeta potentials ranging from 0 to ±30 mV indicate instability, whereas zeta potentials exceeding ±30 mV indicate stability.[24]

3. Transmission Electron Microscopy

TEM (Transmission Electron Microscopy) is a valuable characterization technique for nanoemulsions. It allows for high-resolution imaging of the nanoemulsion droplets, providing information about their size, shape, and internal structure. TEM helps in assessing the uniformity and stability of the droplets, as well as the distribution of encapsulated nanoparticles or active ingredients. It aids in understanding the morphology and interfacial properties of nanoemulsions, supporting their formulation optimization and performance evaluation.[25]

4. FESEM (Field-Emission Scanning Electron Microscopy)

FESEM (Field-Emission Scanning Electron Microscopy) is a powerful imaging technique used for the characterization of nanoemulsions. It provides high-resolution, three-dimensional images of the emulsion droplets, allowing for the examination of their surface morphology and structure. FESEM also enables the investigation of the distribution and localization of nanoparticles or active ingredients within the nanoemulsion. It aids in understanding the interfacial characteristics and particle arrangements, providing valuable insights for the development and optimization of nanoemulsion formulations.[26]

5. Atomic force microscope (AFM):

AFM (Atomic Force Microscopy) is a relatively recent technique utilized to investigate the surface morphology of nanoemulsion formulations. In this technique, nanoemulsions are first diluted with water, and the diluted nanoemulsion is then drop-coated onto a glass slide. The coated droplets are subsequently dried in an oven and scanned using AFM at a scan rate of 100 mV/s. [27]

6. Dye solubilization

A water-soluble dye has the ability to disperse within an oil-in-water (O/W) globule, while it dissolves in the aqueous phase of a water-in-oil (W/O) globule. Conversely, an oil-soluble dye can disperse within a W/O globule but is soluble in the oily phase of an O/W globule. When a water-soluble dye is added to an O/W nanoemulsion, it uniformly incorporates the color throughout the emulsion. However, in a W/O emulsion, the dye remains in the dispersed phase, resulting in uneven distribution of color. This phenomenon can be observed through microscopic examination of the emulsion, revealing the different behaviors of water-soluble and oil-soluble dyes in O/W and W/O nanoemulsions, respectively.[28]

7. Thermodynamic stability studies

Thermodynamic stability investigations are typically conducted in a three-step process. Initially, a heating-cooling cycle is performed to evaluate the impact of temperature variations on the stability of the nanoemulsion. The nanoemulsion is subjected to six cycles alternating between refrigeration temperature (4°C) and room temperature (40°C), with each temperature being maintained for at least 48 hours. Formulations that demonstrate stability under these temperature conditions proceed to the next step: a centrifugation study. In this study, the formulated nanoemulsions are centrifuged at 5000 rpm for 30 minutes to assess for any signs of phase separation, creaming, or cracking. Those formulations that exhibit no indications of instability then undergo a freeze-thaw cycle. In this third step, the nanoemulsion formulations are subjected to three freeze-thaw cycles, with temperatures ranging from -21°C to +25°C. Formulations that remain stable throughout this cycle are considered to have good stability.[29]

8. Determination of viscosity

Viscosity assessment plays a crucial role in the physicochemical characterization of nanoemulsions. Several instruments are utilized for measuring viscosity, including the Ostwald viscometer, Hoeppler falling ball viscometer, Stormer viscometer, Brookfield viscometer, and Ferranti-Shirley viscometer. Among these options, the Brookfield viscometer is commonly preferred for assessing the viscosity of nanoemulsions. The viscosity determination helps determine whether the system is an oil-in-water (O/W) or water-in-oil (W/O) emulsion. Low viscosity indicates an O/W type, while high viscosity suggests a W/O type system. Accurate viscosity measurements contribute to the understanding of the emulsion's composition and behavior.[30]

9. Refractive index

The refractive index is a crucial parameter that indicates how light propagates through a medium and influences the transparency of a nanoemulsion. It is defined as the ratio of the speed of light (c) in a reference medium to the phase speed of light (vp) in the

medium: n = c/vp. The refractive index of a nanoemulsion can be determined using an Abbe-type refractometer at a temperature of 25±0.5°C. A drop of the nanoemulsion is placed on a slide, and its refractive index is compared with that of water (1.333). If the refractive index of the nanoemulsion is equal to that of water, it indicates that the nanoemulsion possesses a transparent nature. This measurement helps assess the optical properties and transparency of the nanoemulsion system.[31]

10. Percentage Transmission

The transparency of a formulated nanoemulsion can be assessed by measuring its percent transmittance at a specific wavelength using a UV spectrophotometer, with distilled water as a reference. If the nanoemulsion demonstrates a percent transmittance exceeding 99%, it is regarded as having a transparent nature. This indicates that the nanoemulsion allows a significant amount of light to pass through without significant absorption or scattering, implying good optical clarity.[32]

11. pH and osmolarity measurements

A pH meter is utilized to measure the pH of a nanoemulsion, while a microosmometer is employed to determine the emulsion's osmolarity using the freezing point method. To perform the osmolarity measurement, a volume of 100 µl of the nanoemulsion is transferred into a microtube, and subsequent measurements are conducted. These characterization techniques provide essential information about the pH level and osmolarity of the nanoemulsion, aiding in understanding its physicochemical properties and potential applications.[33]

12. Fluorescence test

Several oils exhibit fluorescence when exposed to UV light. When a water-in-oil (W/O) nanoemulsion is observed under a microscope with fluorescence lighting, the entire field of view will emit fluorescence. However, in the case of an oil-in-water (O/W) nanoemulsion, fluorescence will appear as distinct spots or localized areas. This phenomenon can be used as a visual indicator to differentiate between W/O and O/W nanoemulsions based on their fluorescence patterns when illuminated with UV light.[34]

***13. in vitro* drug release studies**

In vitro, drug release studies are conducted to estimate the performance of a drug formulation in vivo. The release rate of the drug in vitro is typically investigated using a USP dissolution apparatus. A nanoemulsion or dried nanoparticles containing an equivalent of 10 mg of the drug are dispersed in a buffer and introduced into dialysis membrane pouches, which are then placed in a flask containing buffer solution. The study is conducted at a temperature of 37±0.5°C with stirring at a speed of 50 rpm. At specific time intervals, samples are withdrawn and replaced with the same volume of fresh dissolution medium. These samples are appropriately diluted, and their absorbance is measured using spectrophotometry at a designated wavelength. The absorbance values of the collected samples are then used to calculate the percentage of drug release at different time points by referencing a calibration curve.[35]

Applications of Nanoemulsions:

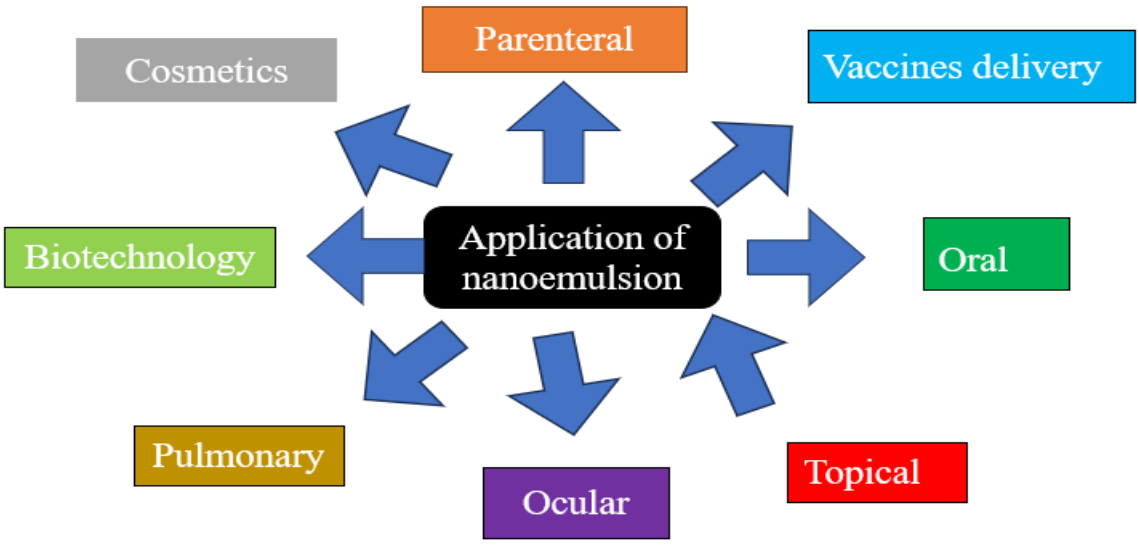

Fig1: application of nanoemulsions.

1. Parenteral administration

Parenteral administration of medications with limited solubility, particularly via the intravenous (IV) route, is a significant concern in the pharmaceutical industry due to poor drug delivery to specific target sites. Nanoemulsion formulations offer advantages over macroemulsion systems when administered parenterally, as the small particle size of nanoemulsions leads to slower and more sustained excretion from the body compared to emulsions with larger particles. This results in longer duration of action. Parenteral delivery can be achieved using either oil-in-water (o/w) or water-in-oil (w/o) nanoemulsions. Various nanoemulsion systems described in the literature show potential for parenteral administration, with consideration given to surfactant toxicity and the suitability of parenteral use.[36]

2.Oral delivery

Nanoemulsion formulations offer several advantages for oral drug delivery compared to traditional formulations. They have the potential to increase the clinical effectiveness and absorption of medications, while reducing drug toxicity. Nanoemulsions have shown promise as a delivery system for various medications, including steroids, hormones, diuretics, antibiotics, and peptides. Peptides and proteins, which are highly potent and targeted in their physiological effects, are often challenging to deliver orally. Conventional formulations have low oral absorption rates (below 10%) for these molecules. Nanoemulsions have the potential to improve the oral bioavailability of protein drugs, reducing the reliance on parenteral administration.[37]

3. Topical administration

Topical drug administration offers advantages such as bypassing hepatic first-pass metabolism and enabling direct application to the affected skin or eyes. In the case of prostaglandin E1 administration, both oil-in-water (o/w) and water-in-oil (w/o) nanoemulsions were tested in a hairless mouse model. The nanoemulsions were formulated using oleic acid or Gelucire 44/14 and stabilized with a surfactant mixture of Labrasol and PlurolOleique CC 497. Although the o/w nanoemulsion demonstrated enhanced drug delivery rates, the penetration rates of both systems were deemed insufficient for practical application. Additionally, a lecithin/IPP/water nanoemulsion was used to deliver indomethacin and diclofenac transdermally. Through FTIR spectra and differential scan calorimetry (DSC), it was observed that the IPP organogel altered the lipid composition in the mammalian stratum corneum after one day of incubation.[38]

4. Ocular and pulmonary drug delivery

Topical administration is the primary method for delivering drugs to treat eye disorders. In ocular delivery, researchers have investigated o/w nanoemulsions to address challenges such as poor solubility, increased drug absorption, and achieving sustained release. Nanoemulsions containing pilocarpine were formulated using ingredients like lecithin, propylene glycol, and PEG 200, with IPM as the oil phase. These formulations exhibited favorable properties such as a suitable refractive index and low permeability, making them well-suited for ophthalmic applications. Additionally, a non-ionic fluorocarbon surfactant was utilized to stabilize a water-in-HFA propellant nanoemulsion designed for pulmonary delivery.[39]

5. Nanoemulsions in Biotechnology

Enzymatic and biocatalytic processes often utilize aqua-organic or purely organic media, including biphasic systems. Pure polar media can lead to the denaturation of biocatalysts. However, using water-resistant media offers several advantages. Enzymes with low water content.[40]

- Exhibit increased solubility in non-polar reactants.
- Experience thermodynamic equilibrium modifications that promote condensation reactions.
- Show improved thermal stability, enabling reactions to be conducted at high temperatures.

6. Future perspectives

Nanoemulsions have emerged as promising drug delivery systems in the field of pharmacy due to their ability to solubilize non-polar active compounds. They offer numerous advantages and diverse applications in therapeutics and cosmetic formulations for hair and skin. In drug delivery, nanoemulsions serve as efficient carriers for bioactive substances, enabling administration through various routes. For oral drug delivery, the absorption in the gastrointestinal tract is influenced by the droplet size of the nanoemulsion. With the growing interest in herbal drug formulations, nanoemulsions hold great potential as a delivery platform for challenging phytopharmaceuticals. The future of nanoemulsions relies on the innovative formulation approaches that leverage their advantages to address issues related to drug absorption, permeation, and stability, both for conventional and herbal drugs.[41]

Conclusion:

Nanoemulsions, composed of surfactant, co-surfactant, and oil, are stable fluid mixtures with translucency and isotropic properties. They provide an efficient dosage form for protecting labile drugs, controlling drug release, enhancing the solubility of poorly water-soluble drugs, improving bioavailability, and reducing patient variability. They can be formulated for various administration routes, making them versatile in pharmaceutical applications. The stability of nanoemulsion formulations can be enhanced by controlling factors such as surfactant and co-surfactant types and amounts, oil phase variations, formulation techniques, and process variables. Overall, nanoemulsion formulations offer effective, secure, and patient-compliant delivery methods for pharmaceuticals. They also hold the potential for overcoming absorption challenges and enhancing the miscibility of phytopharmaceuticals with cell membrane lipids.

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