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Microemulsions as a potential carrier for improved drug delivery

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ABSTRACT: Microemulsions are thermodynamically stable colloidal dispersions formed in an oil-water environment with the help of surfactants. They are transparent or translucent, isotropic, and have a small droplet size, typically 10 to 100 nanometers. In the pharmaceutical industry, microemulsions are often used to enhance the solubility of poorly soluble drugs. Many drugs have low aqueous solubility, leading to poor bioavailability and reduced therapeutic efficacy. However, when formulated as microemulsions, these drugs can be solubilized in the oil-water interface of the microemulsion system, resulting in a significant increase in their apparent solubility. The small droplet size and large interfacial area of microemulsions provide an ideal environment for incorporating hydrophobic drugs, as the drug molecules can be accommodated in the hydrophobic core of the micelles or droplets. This solubilization makes the drug more readily available for absorption in the body, thereby improving its bioavailability. As thermodynamically stable colloidal dispersions, microemulsions have gained significant attention due to their unique properties and versatile applications. This review paper aims to provide a comprehensive overview of microemulsions with respect to its patentability arena, delving into nuanced aspects that have not been extensively covered in prior review articles. We address key unanswered questions in the existing literature, offering fresh perspectives and insights. Our analysis encompasses the latest advancements in microemulsion research, highlighting novel applications, formulation strategies, emerging trends, market potential of microemulsion as well as its future scope in the pharmaceutical industry.

KEYWORDS: Microemulsion; Ternary phase; solubilization; applications; co-solvents.

1. INTRODUCTION

Microemulsion-based drug delivery systems have emerged as a promising avenue in pharmaceutical research, offering unique advantages in solubility enhancement, bioavailability, and targeted drug delivery. The dynamic nature of microemulsions, characterized by their thermodynamic stability and nanoscale droplet size, presents an attractive platform for overcoming challenges associated with poorly water-soluble drugs. This introduction seeks to provide an insightful overview of the current state of research on microemulsion drug carriers, building upon key findings from recent studies in the field.

Microemulsions are transparent because their droplet size is significantly smaller than 25% of the wavelength of visible light. The microemulsion can be easily formed and occasionally happens on its own, typically without the need for intense energy input. In numerous instances, a supplementary cosolvent or cosurfactant is employed along with the surfactant, water phase, and oil phase [1]. The process of creating coarse emulsions demands a substantial amount of energy input, whereas the production of microemulsions requires significantly less energy. The production of microemulsions is characterized by its speed and spontaneity, allowing for the easy inclusion of thermo-sensitive drugs at the onset without the fear of deterioration. The microemulsions have a clear and uniform appearance which allows for easy analysis using spectroscopic techniques. One of the key features of microemulsions is their remarkable stability, which prevents any process of phase separation. Additionally, they offer the advantage of a controlled drug release rate, slow degradation, and most importantly, targeted specificity [2].

Previous investigations into microemulsion drug delivery have illuminated several crucial aspects. Notably, Badawi *et al.,* (2023) and Priyadarshini et al., (2023), demonstrated the successful encapsulation of tazarotene and mefloquine in essential oil-based microemulsion formulation using either Jasmine oil or

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Jojoba oil and pomegranate oil, black cumin seed oil, garlic oil, respectively leading to a remarkable increase in drug bioavailability in preclinical models for the treatment of acne vulgaris and malaria respectively. Panchal *et al.*, (2023) also worked on novel krill oil-based clomiphene microemulsion as a therapeutic strategy for polycystic ovary syndrome treatment. This groundbreaking study laid the foundation for subsequent explorations into the potential of essential oils to be used in microemulsions as effective drug carriers [3-5]. Additionally, the work of Szumala and colleagues (2023) shed light on the influence of surfactant composition on the stability and performance of microemulsions, providing valuable insights into formulation optimization strategies [6]. Despite these strides, there exists a compelling need for a comprehensive synthesis of the diverse findings in this rapidly evolving field.

Building upon the seminal contributions of these studies, our review paper aims to consolidate and critically analyze the latest advancements in microemulsion drug delivery. By synthesizing findings from disparate sources, we aim to identify key knowledge gaps and areas warranting further investigation. This review not only serves to elucidate the current landscape of microemulsion drug carriers but also endeavors to push the boundaries of existing knowledge, offering a roadmap for future research endeavors in this exciting and transformative domain.

1.1. Advantages [7-10]

i. Microemulsions enhance the solubility of medications, allowing for improved absorption and bioavailability.
ii. They exhibit supersolvent properties, facilitating the dissolution of higher drug concentrations than conventional formulations.
iii. Microemulsions are thermodynamically stable, ensuring consistent drug delivery and avoiding phase separation issues.
iv. The self-emulsifying nature of microemulsions simplifies the formulation process, making them user-friendly for pharmaceutical applications.
v. The use of microemulsions can lead to improved drug efficacy due to enhanced drug solubility and absorption.
vi. Microemulsions can reverse drug crystallization, preventing the formation of unwanted precipitates and ensuring formulation stability.
vii. Significantly less energy is required for the production of microemulsions compared to some alternative formulations, making the process more efficient.
viii. Microemulsions serve as effective carriers for both hydrophobic and hydrophilic drugs, offering versatility in drug delivery systems.

1.2. Disadvantages [11-13]

i. Microemulsions may pose challenges related to stability, with issues such as phase separation or droplet coalescence impacting their shelf life.
ii. The ability of microemulsions to dissolve high-melting substances is limited, which can constrain their applicability for certain drugs or formulations.
iii. A drawback of microemulsions is the requirement for a significant amount of surfactant, which may raise concerns regarding potential toxicity or formulation costs.
iv. The stability of microemulsions is susceptible to variations in temperature and pH, necessitating careful storage conditions and potentially affecting their performance in different environments.

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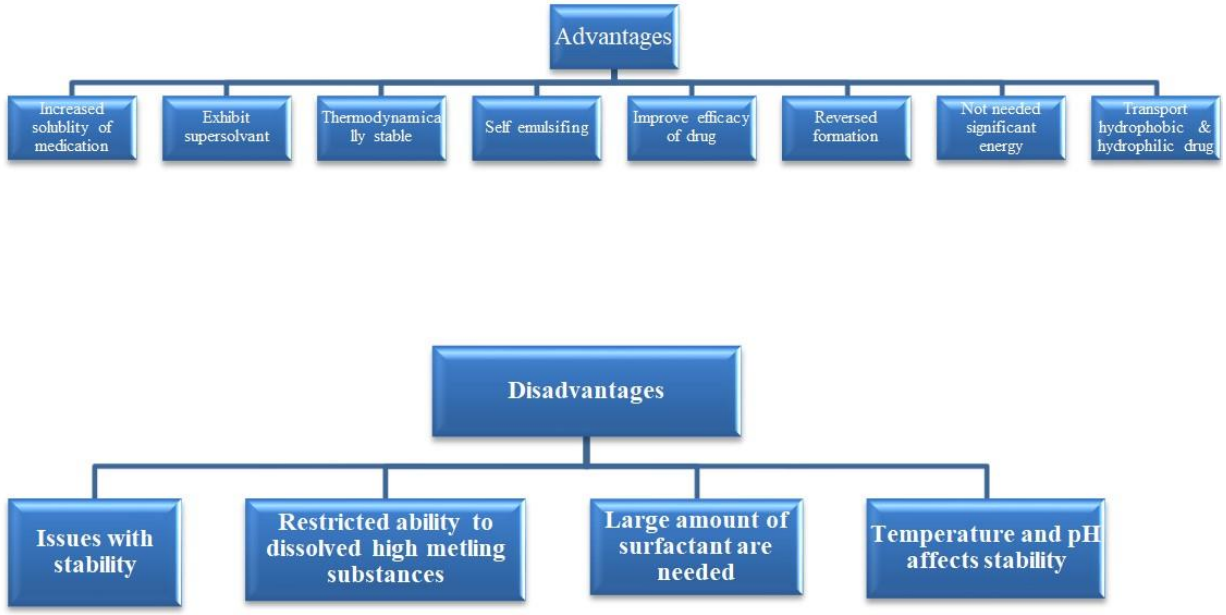

Figure 1. Advantages and disadvantages of microemulsions

2. COMPOSITION

2.1. Oil phase

Oil is described as a liquid with minimal polarity and minimal ability to mix with water. Cyclohexane, mineral oil, toluene, and vegetable oil are all examples of this type of phase. Oil plays a vital role in microemulsion as it enables effective solubility of lipophilic drugs and enhances the fraction of these drugs that are carried through the intestinal lymphatic system. Oil is described as a liquid that exhibits low polarity and limited ability to mix with water [13].

Oily drugs are more effectively dissolved in microemulsions with an oil-in-water composition. The crucial factor for choosing the oil phase is that the drug must be highly soluble in it, the ability of the oil component to enter and expand the tail group area of the surfactant monolayer affects its curvature. Shorter chain oils can enter the tail group area more deeply in comparison to longer chain alkanes, leading to a more significant expansion of this zone. As a result, there is higher negative curvature, which in turn decreases the effective HLB. The properties of penetration enhancement have been extensively investigated for both saturated fatty acids, (such as lauric, myristic, and capric acid); as well as unsaturated fatty acids (including oleic acid, linoleic, and linolenic acid). Fatty acid esters derived from lauric, myristic, and oleic acid, specifically in the forms of ethyl and methyl esters, have been utilized as the oil component [14].

2.2. Aqueous phase

Typically, the water-based component comprises hydrophilic active substances and preservatives. Buffer solutions can be employed as an aqueous phase on certain occasions.

2.3. Surfactants

Surfactants are made up of a polar head group and a non-polar tail. They are molecules with a powerful chemical dipole that can form microstructures and are active on the surface. These substances can have characteristics of ionic nature, either anionic or cationic charged, non-ionic or zwitterionic. Surfactant molecules undergo self-association due to a combination of inter-molecular and intra-molecular forces, along with considerations of entropy. Surfactant molecules exhibit versatility in their structural arrangements. Micelles can adopt various shapes such as spheres, rods, hexagons (made of rods), lamellar (sheets), reversed micelles, or reversed hexagonal micelles [15].

Surfactants are classified into four types; non-ionic surfactant, zwitterionic surfactant, cationic surfactant, and anionic surfactant [16]. Surfactants, whether they be of the ionic or nonionic variety, play a

crucial role as a stabilizing factor in the preparation of microemulsions. Generally, nonionic surfactants and cosurfactants are utilized to develop microemulsions that are kept stable through a hydration layer formed on the hydrophilic surface using hydrogen bonding or dipole moment [17].

The microemulsion's stability can be influenced by the HLB value and indicates that the surfactant's hydrophilic and lipophilic entities have a moderate impact. The formation of w/o microemulsions is typically associated with low HLB grades ranging from 3 to 6, whereas high HLB grades between 8 and 18 are commonly associated with the formation of o/w microemulsions (Table 1) [18].

HLB is a profitable time-tested device utilized by formulators to choose the leading surfactants from the numerous hundreds accessible to different Surfactants And oils. It is important for surfactant selection. HLB values of some surfactants and oils are given in Table 2 [19].

Table 1. HLB scale [18]

HLB value	Uses
<3	Surface film
3–6	Water-in-oil emulsifiers
7-9	Wetting agent
8-15	Oil-in-Water emulsifiers
13-15	Detergents
15-18	Solubilizes

Table 2. HLB value of different Oils and Surfactant [19]

Name of surfactant	HLB
Sorbitan laurate (Span 20)	8.6
Sorbitan palmitate (Span 40)	6.7
Sorbitan stearate (Span 60)	4.7
Sorbitan oleate (Span 80)	4.3
Sorbitan trioleate (Span 85)	1.8
Polyoxyethylene sorbitan laurate (Tween 20)	16.7
Polyoxyethylene sorbitan palmitate (Tween 40)	15.6
Polyoxyethylene sorbitan stearate (Tween 60)	14.9
Polyoxyethylene sorbitan oleate (Tween 80)	15.0
Polyoxyethylene sorbitan trioleate (Tween 85)	11.0
Brij 30	9.5
Brij 35	16.9
Sodium oleate	18.0
Potassium oleate	20.0

2.3.1. Cationic surfactants

Cationic surfactants are substances that, when mixed with water, split into two parts: an amphiphilic cation and an anion, typically of the halogen variety. A significant portion of this group comprises nitrogen compounds like salts of fatty amines and quaternary ammonium. These compounds typically possess one or more elongated alkyl chains derived from natural fatty acids. Among them, alkylammonium halides and tetra-alkylammonium halides are the prevalent types. Alkyl ammonium halides exhibit remarkable hydrogen bonding capabilities and form highly robust interactions with water molecules. Cetyltrimethylammonium bromide (CTAB) and didodecyldimethylammonium bromide (DDAB) are among the most widely recognized cationic surfactants. In general, these particular surfactants are costlier than anionic surfactants due to the need for a high-pressure hydrogenation process during their production [20].

2.3.2. Anionic surfactants

Surfactants in water create an amphiphilic anion and cation, typically consisting of an alkaline metal (such as Na or K) or quaternary ammonium, particularly when anionic materials are present. The anionic

charge of these surfactants stems from the presence of an ionized carboxyl group. Approximately 50% of the world's total production comes from anionic surfactants. The most common type of anionic surfactants that can be found is referred to as soaps, which are alkali alkanoates. Regarding both form and operation, this is the most familiar type of surfactant. Among these surfactants, the carboxylate, sulfonate, and sulfate groups hold utmost significance as they form the three main anionic groups [21].

2.3.3. Non-ionic surfactants

The hydrophilic surface of non-ionic surfactant remains stable through its interaction with the hydration layer of water, primarily via dipole and hydrogen bonds. Their hydrophilic components, such as phenol, alcohol, ester, or amide, are not dissociable, which prevents them from ionizing in an aqueous solution. Most nonionic surfactants possess hydrophilic properties because of the inclusion of a polyethylene glycol chain [13].

2.3.4. Zwitterionic surfactants

Zwitterionic surfactants possess positively as well as negatively charged moieties and can generate microemulsions through the addition of co-surfactants. Zwitterionic surfactants, such as lecithin, which are commonly found in soybeans or eggs, are composed of phospholipids. In contrast to other ionic surfactants that may possess some level of toxicity, lecithin, a substance that predominantly consists of diacyl phosphatidylcholine, exhibits exceptional biocompatibility. Betaines, including alkyl betaines and heterocyclic betaines, are another significant group of zwitterionic surfactants [13]. Emulsifying agents are classified based on charged groups as shown in Table 3.

2.4. Co-surfactants

A variety of surfactants, either single-chain or double-chain, can be utilized in the production of microemulsions. Co-surfactants reduce the interfacial tension between oil and water. Sulfosuccinates, which are surfactants with two chains, can create microemulsions even without cosurfactants. However, due to their high level of toxicity, they are not recommended for use in pharmaceuticals. Although cosurfactants are essential for creating microemulsions, they have demonstrated harmful effects, such as in the case of medium chain-length alcohols. Therefore, it is crucial to carefully select appropriate surfactants and cosurfactants [23]. Some examples of cosurfactants are propylene glycol 400, caproyl 190, propylene glycol, PEG 400, n-butanol, propylene glycol, ethanol, and transcutol P [24].

3. METHOD OF PREPARATİON

3.1. Phase titration method (Spontaneous emulsification method)

The creation of microemulsions uses the method of spontaneous emulsification, also known as the phase titration method, and can be visually illustrated through the use of phase diagrams. Developing a phase diagram can be an effective method for examining the intricate array of interchanges that may take place when various components are combined. Multiple association structures, such as emulsions, micelles, lamellar, hexagonal, cubic, and numerous kinds of gels and oily dispersion, are created through the chemical composition and concentration of each element, leading to the formation of microemulsions. It is crucial to comprehensively comprehend the phase equilibria and accurately classify the phase boundaries in this research. Because the quaternary phase diagram is challenging to read and takes a lot of time to create, the frequently utilized pseudo-ternary phase diagram identifies specific zones, like the microemulsion zone. Each corner of the diagram depicts 100% of a specific component. The separation of the region into either w/o or o/w microemulsion can be easily determined based on the composition, specifically if it contains rich oil or water. It is important to conduct observations with precision to avoid the incorporation of metastable systems [25].

Table 3. Classification of emulsifying agents based on the presence of formally charged groups in their heads [22]

Sr.	Surfactant class	Surface charge	Example
1	Anionic (based on sulfate, sulfonate or carboxylate anions)	Negative	-Perfluorooctanoate (PFOA or PFO) -Perfluorooctanesulfonate (PFOS) -Sodium dodecyl sulfate (SDS), ammonium lauryl sulfate, and other alkyl sulfate salts -Sodium laureth sulfate, also known as sodium lauryl ether sulfate (SLES) -Alkyl benzene sulfonate -Soaps, or fatty acid salts
2	Cationic (based on Quaternary ammonium cations)	Positive	-Cetyl trimethylammonium bromide (CTAB) a.k.a. hexadecyl trimethyl ammonium bromide, and other alkyl trimethyl ammonium salts -Cetylpyridinium chloride (CPC) -Polyethoxylated tallow amine (POEA) -Benzalkonium chloride (BAC) -Benzethonium chloride (BZT)
3	Zwitterionic (amphoteric)	Two oppositely charged groups	-Dodecyl betaine -Cocamidopropyl betaine -Coco ampho glycinate
4	Nonionic	No charge groups	-Alkyl poly(ethylene oxide) -Alkylphenol poly(ethylene oxide) -Copolymers of poly(ethylene oxide) and poly(propylene oxide) (commercially called Poloxamers or Poloxamines) -Alkyl poly glucosides, including octyl glucoside and decyl maltoside -Fatty alcohols, including cetyl alcohol and oleyl alcohol -Cocamide MEA -Polysorbates, including Tween 20 and Tween 80

3.2. Phase inversion method

The microemulsion leads to a phase inversion when the dispersed phase is excessively added or due to temperature changes. During phase inversion, significant physical transformations occur, resulting in modifications of particle size that may negatively affect drug release in both laboratory and living systems. These techniques involve modifying the innate curvature of the surfactant. To achieve this for non-ionic surfactants, the system's temperature can be modified, prompting a shift from a low-temperature oil-in-water microemulsion to a high-temperature water-in-oil microemulsion. As the system cools, it reaches a moment where spontaneous curvature becomes zero and surface tension becomes insignificant, allowing the formation of fine-distributed droplets of oil. The technique is commonly referred to as the method of temperature inversion during the phase conversion process. Instead of focusing solely on temperature, other factors such as pH level or salt content could also be taken into account. Furthermore, modifying the proportion of water in the system can result in a change in the natural curvature radius transition. The addition of water into oil results in the creation of predominantly discrete water droplets within the ongoing oil phase. By altering the proportion of water, the natural curvature of surfactants shifts from primarily stabilizing microemulsions of water in oil to those of oil in water when reaching the inversion point. Surfactants with shorter chains create adaptable monolayers at the interface between o/w, leading to the formation of a bicontinuous microemulsion when the inversion point is reached [26].

4. EVALUATION PARAMETERS

4.1. Dilution test/miscibility test

In the miscibility test, an uninterrupted component, such as a continuous phase is introduced. If an o/w emulsion is exposed to continuous additions of water, it will remain stable but if unlimited amounts of oil are added, the emulsion will lose its stability and the oil will separate from the mixture. On the contrary, w/o emulsion is an opposite scenario.

4.2. Viscosity Measurement

At 25˚C, a digital viscometer was utilized to determine the viscosities of the microemulsion [27].

4.3. pH

pH is a crucial factor when it comes to nanoemulsion. The pH of the final preparation and, accordingly, the mode of application is dependent on the excipients utilized in the formulation. A modification in the pH level can impact the zeta potential of the mixture, potentially leading to an adverse impact on the formulation's stability. The pH level of the compositions was assessed using a digital pH meter. The data was collected three times and then an average of the results was considered [28].

4.4. Polarized light microscopy

A microscope made by Nikon Inc., specifically the Optiphot-Pol NIKON 144850 model. A camera-equipped mic was utilized in Garden City, NY, for examining the different stages of the phase diagram and confirming the homogeneous behavior of microemulsions. Under polarized light, an examination was carried out by placing a small quantity of the specimen between a glass slide and a coverslip. Photographs were captured with a magnification of 10X and 20X [29].

4.5. Entrapment efficiency (EE)

The % EE was calculated by promptly centrifuging newly prepared w/o/w multiple emulsions at 4000 rpm for 10 minutes. Using a hypodermic syringe, an accurate amount of the aqueous phase (which is the lower layer) measuring 1ml was extracted and suitably mixed with phosphate buffer 6.8 after dilution. The millipore filter (0.22 mm) was used to filter the solution, and the drug content was examined with a UV spectrophotometer at 247.6 nm. To determine the encapsulation efficiency, equation 5 was utilized [30].

$$\% \text{ EE} = \frac{[\text{Total drug incorporated} - \text{Free Drug}]}{\text{Total drug}} \times 100$$

4.6. Particle size evaluation

The size and distribution of droplets in various Amphotericin B microemulsions were measured using photon correlation spectroscopy with the Malvern S zetamaster. To analyze the samples, the drug-loaded microemulsions were diluted with the external aqueous phase at a 1:5 (v/v) ratio and filtered through 0.45 mm filters before being examined. All recorded values were taken at a temperature of 25˚C. Each sample underwent 10 runs with a fixed detection angle of 90° to measure the intensity of scattered light [31].

4.7. Partition coefficient (P)

The investigation on partition coefficient was carried out by utilizing n-octanol as the oil component and a saline phosphate buffer with a pH value of 7.4 as the aqueous phase. An equal quantity of both phases was combined and mechanically shaken in a water bath shaker for 24 hours before the experiment until saturation was achieved. The centrifugal force of 2000 rpm was utilized to isolate the saturated stages. 10 mL of each phase were measured and transferred into separate conical flasks to ensure equal volume. The experiment involved introducing 100 milligrams of precisely measured drug into a flask, which was then shaken for 6 hours at a temperature of 32˚Cand a speed of 100 rpm to ensure complete partitioning. After being subjected to centrifugation for 5 minutes at 1000 rpm, the two phases were separated. The spectrophotometric analysis was carried out on the buffer phase to determine the drug concentration. The drug's concentration in octanol was determined as the discrepancy between its initial and ultimate concentrations in the buffer phase. The formula for finding the partition coefficient (P) of the drug Ko/w

involved determining the concentration in octanol and concentration in phosphate buffer pH 7.4, and then plugging those values into the equation. The resulting P value was used to calculate Log P [32].

4.8. Interfacial tension

One can gain insights into microemulsion creation and characteristics by calculating interfacial tension. The phase behavior in low ultra-values is associated with interfacial tension, which reveals the presence of a surfactant or middle-phase microemulsions in equilibrium with oil and aqueous phases. The measurement of ultra-low interfacial tension can be done utilizing the spinning-drop apparatus. These characteristics are obtained by analyzing the shape of a drop containing a low-density phase, which is rotated within a cylindrical capillary containing a high-density phase [33].

4.9. Staining test/dye-solubility test

A drop of methylene blue solution, which can dissolve in water, measuring 10 microliters was introduced into the emulsion. If the emulsion is water-based with an oil phase, the dye will smoothly dissolve in the whole structure. If the emulsion is oil-based with a water phase dispersed throughout, the dye will gather in a cluster on the surface of the mixture [34].

4.10. Differential scanning calorimetry (DSC)

The thermal analysis can be conducted using a mettler toledo DSC822. The specimens underwent a gradual cooling process from 25 to -50˚C, decreasing at a rate of 5 ˚C per minute, and were maintained at -50 ˚C for 3 minutes before being swiftly heated up to 50 ˚C at a rate of 10 ˚C per minute. The process of heating was executed in an environment that accommodated nitrogen gas flowing at a velocity of 50 ml/min [35].

4.11. Centrifuge stress test

The centrifuge was used to spin the systems at 1,073 times gravity (4,000 rpm) for a duration of 15 minutes. Following this, phase separation can be assessed [36].

4.12. Freeze thawing method

The stability of the formulations was assessed using the freeze-thaw method. The mixtures were exposed to 3-4 rounds of freeze-thaw cycles that consisted of being frozen at -4°C for 24 hours and then thawed at 40°C for 24 hours. The substances were also centrifuged for 5 minutes at 3000 rotations. The formulations that were chosen for further investigations were those that exhibited stability toward phase separation [37].

5. PHARMACEUTİCAL APPLICATIONS

5.1. Oral applications

Consequently, microemulsion has been identified as an optimal channel for dispensing pharmaceuticals like steroids, hormones, diuretics, and antibiotics. While peptides and proteins are incredibly effective in their physiological abilities, administering them through the oral route can prove to be challenging. In traditional methods, the uptake of medication through the mouth is limited in its effectiveness. Typically, formulations without microemulsions that contain less than 10% of the active ingredient are not effective for oral consumption in terms of providing therapeutic benefits. The majority of protein drugs are solely accessible as parenteral formulations due to their limited ability to be absorbed orally. Peptide drugs necessitate multiple dosing due to their brief biological half-life when administered through a parenteral route [38]. The administration of microemulsion formulations orally has numerous advantages in comparison to traditional oral formulations, such as enhanced absorption rate, improved therapeutic effectiveness, and reduced drug toxicity [39].

5.2. Topical applications

The topical application of medications can offer various benefits compared to other methods because it helps prevent the drug's hepatic first-pass metabolism and its resulting damaging effects. The second advantage pertains to the efficient administration and precise placement of medication directly to the impacted region of the dermis or ocular surface. The efficiency of both o/w and w/o microemulsions in administering prostaglandin E1 53 has been analyzed in a hairless mouse model [40].

Despite finding improvements in delivery rates with the o/w microemulsion, the authors ultimately deemed the penetration rates insufficient for pragmatic application with either system. It has been reported that lecithin/IPP/water microemulsion has been utilized for transdermal transportation of indomethacin and diclofenac. The interruption of lipid organization in the stratum corneum of humans was observed after one-day incubation of utilizing IPP organogel, as indicated by Fourier transform infrared spectroscopy and DSC [41].

5.3. Parenteral applications

Developing injectable forms for both lipid and water-soluble medicines has been a challenging task. The use of w/o microemulsions is advantageous for delivering poorly soluble medications intravenously, eliminating the need for administering suspensions. Maintaining a high dosage is necessary for regular medication. Plasma has demonstrated superior physical stability compared to liposomes and other carriers, with the added advantage of increased resistance against drug leakage from the internal oil phase. Parenteral delivery of sparingly soluble drugs has been made possible through the development of o/w microemulsions. Von Corsewant and Thoren adopted a different method by substituting C3-C4 alcohols with co-surfactants that are suitable for parenteral use, such as polyethylene glycol (400)/polyethylene glycol (600) 12-hydroxy stearate/ethanol. This allowed for the maintenance of a flexible surfactant film and the formation of a spontaneous curvature close to zero, resulting in the generation of microemulsions with a nearly evenly balanced middle phase [42]. Numerous literature sources have documented the application of water-in-oil (w/o) microemulsions as a vehicle for delivering water-soluble substances via intramuscular means. If the microemulsion is absent, undergoing phase inversion becomes a noteworthy characteristic that yields an o/w microemulsion that can serve as a viable option for delivering parenteral drugs [43].

5.4. Ophthalmic applications

The dexamethasone eye drop formulated with microemulsion is easily tolerated by the eye and provides improved bioavailability [44]. The enhanced system displayed improved permeation into the eye, presenting the potential to reduce the frequency of eye drop usage per day. The study examined microemulsion systems containing retinol and its esters as the oil component, along with surfactants including tween 80, tween 60, and soybean lecithin, as well as cosurfactants like n-butanol, triacetin, and propylene glycol for delivery to the eye. The composition with the best ophthalmic properties, including refractive index, viscosity, pH, and osmotic tension, was determined to be the most effective for drug delivery. For a duration of 6 months at a temperature of 20˚C, no visible alteration was noticed and the substance was well-tolerated by the body [45].

5.5. Nasal applications

Currently, microemulsions are being examined as a method of administering drugs more effectively through the nasal mucosa. Mucoadhesive polymers aid in increasing the duration of their stay on the mucosal surface. Lianly and her colleagues; explored the impact of diazepam on the immediate response to status epilepticus. They discovered that the uptake of diazepam through the nose was swift when administered at a dose of 2 mg kg-1, with the highest level of the drug in the blood plasma achieved within 2 to 3 minutes [46].

6. PATENTS

Patent no	Title	Inventors	Applicant	Claims	Composition	Ref
5,376,397	Microemulsions of oil and water	Anilkumar G. Gaonkar, Vernon Hills,	Kraft General Foods, Inc	(1) A type of oil that does not create microemulsions when combined with water and one of the alcohols in the group including ethanol, propylene glycol, glycerin, sugar, alcohol, or a combination of these substances. 2. hydrophilic surfactant, is typically found in amounts ranging from 20 to 35% by	Ethanol, propylene glycol, glycerine, sugar, Sugar alcohol, and hydrophilic surfactant, water-miscible	[47]

				weight. 3. The first emulsifying agent water miscible alcohol, is present in the mixture at a concentration between 10% and 15% by weight. Another emulsifying agent is water immiscible alcohol which is present in the amount of approximately level 5-15% by weight, etc.	alcohol emulsifying agent, water in miscible alcohol emulsifying agent, water.	
US 8,158,134 B1	Microemulsion preconcentrate, microemulsion, and use thereof	Andreas Supersaxo, Marc Antoine Weder, Georg Weder,	Vesifact AG, Baar (CH)	1. A microemulsion preconcentrate composition consisting of. (a) a mixture containing (i) a fatty acid triglyceride, fatty acid in which caprylic or capric acid, and (ii) either an omega-9 or omega-6 fatty acid. (b) A surface-active component consisting of a polyoxyethylene-based tenside makes up 20 to 80% of the total weight. This substance is mostly free from any elements that can mix with water or dissolve in it. Its composition includes polycarboxylic acids that have undergone esterification with C1-C10 alcohols, as well as esterification products of polyols with C2-C11 carboxylic acids, both of which have 2-10 carboxyl or hydroxy groups.	preconcentrates that contain (a) a mixture that consists of a medium-chain triglyceride and an omega-9 fatty acid and/or an omega-6 fatty acid; and (b) a Surface-active component that contains a polyoxyethylene tenside	[48]
4,146,499	Method for preparing microemulsions	Henri l. Rosano,	Rosano Henri L	A strategy for scattering a water-immiscible liquid in aqueous media as a microemulsion 2. A solution of water-immiscible liquid and primary surfactant is scattered into the liquid media to make a lactescent emulsion and said secondary surfactant is added to the lactescent emulsion to make a microemulsion etc.		[49]
5683625	Method of preparing microemulsions	Marianne D.Berthiaume, James.H.merrifield	General Electric Company	1. A procedure for developing a transparent microemulsion 2. The quantity of surfactant ranges from approximately 1 to 20 parts per hundred of the entire Composition of the microemulsion 3. Inversion phase the temperature of said surfactant ranges from around 50° C. to about 95° C. 3. weight is substantially equal to the weight of said silicone.		[50]

etc [50]

7. MARKET POTENTIAL

The heterogeneous microemulsions are considered steady concerning emulsions and hold a major share within mechanical applications such as formulation. They moreover discover applications in pharmaceuticals owing to their particular properties such as stability, liking towards solubilization, improved compatibility, drug delivery, and gene delivery to cells for disease determination and treatment. moreover, microemulsions play a vital ingredient in cancer treatment. In this setting, the utilization of bio-degradable surfactants in microemulsions turns the complete framework into an economical system. microemulsions are utilized in pharmaceutical applications for oral and topical delivery of a wide extend of products. These incorporate anti-infective, cardiovascular, dermatological products, gastrointestinal drugs, solubilization, and stabilization of dynamic fixings among others.

Table 4. FDA-approved marketed products

Drugs	Brand name	Manufacturer	Therapeutic used	Ref
Cyclosporine	Neoral	Novartis	Immunosuppressant	[51]
Ritonavir	Norvir	Abbott	AIDS	
Diazepam	Diazemuls	Braun Melsungen	Sedation	
DexamethazonePalmitate	Limethason	Green Cross	Corticosteroid	
Propofol	Propofol	Baxter Anesthesia	Anesthesia	
Vitamins A, D, E, and K	Vitalipid	Kabi	Nutrition	
Prostaglandin-E1	Liple	Green Cross	Vasodilator	
Propofol	Diprivan	AstraZeneca	Anesthesia	

8. FUTURE PROSPECTS

Microemulsions have tremendous and significant potential in drug delivery as well as within the industrial process. researchers are working in this field for drug release, coatings, dyes, agrochemicals, and in chemical response. within the prospects, microemulsions will be utilized in the synthesis of nanoparticles and as industrial chemical sensors. the part of microemulsion in giving novel solutions to overcome the issues of poor aqueous solvency of exceedingly lipophilic medicate compounds and give high, more steady, and reproducible bioavailability. topical products are presently utilizing the microemulsion innovation and are likely to develop microemulsion in today's world can be acknowledged as full of potential in a novel drug delivery system

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