Microemulsion: Revolutionizing Drug Delivery with a Novel Approach

Pooja sood[1], Aman Kapoor[2], Preeti Verma[3], Puneet Kumar[4], Panshul Sharma[5*],Gurinder Singh[1], Shubham Garg[6]

[1]Institute of Pharmaceutical Sciences, Bhaddal, Punjab
[2]SVS Paramedical College, Rajouri, (J&K)
[3]Vinayaka College of Pharmacy, Kullu (H.P.)
[4]Dreamz College of Pharmacy, Mandi, (H.P).
[*5]IEC School of Pharmacy, IEC University, Baddi (H.P)
[6]Laureate Institute of Pharmacy, Kathog(H.P)

Abstract:

Microemulsion is an extraordinary dispersion that demonstrates both thermodynamic stability and optical transparency. Unlike conventional emulsions, which often separate into distinct phases, microemulsion forms a single-phase isotropic system that appears uniform and transparent. This exceptional stability is a result of the intricate arrangement of oil, water, and surfactant molecules, which spontaneously organize to minimize interfacial tension and facilitate the formation of a stable colloidal system.

The widespread applications of microemulsion have contributed to its significant recognition across various industries. Its unique properties and behavior have opened doors for advancements in enhanced oil recovery, combustion processes, cosmetics, pharmaceutical formulations, agriculture, metal cutting, enzymatic catalysis, and even organic and bio-organic reactions. The versatility of microemulsion has captivated researchers and industrialists alike, driving continuous exploration and innovation in harnessing its immense potential.

1. Introduction:

A microemulsion is a dispersion composed of water, oil, and surfactant, forming a stable and anisotropic system. The dispersed

domain diameter of microemulsions typically ranges from approximately 1 to 100 nm, commonly 10 to 50 nm. These liquid mixtures, which can also include a co-surfactant, are thermodynamically stable and appear clear. The "oil" component may consist of a complex mixture of various hydrocarbons and olefins, while the aqueous phase can contain salts and other ingredients.[1-3]

The term "microemulsion" refers to a system with at least three components: an oily phase, an aqueous phase, and a surfactant. In some cases, a co-surfactant is also present. The microstructure of microemulsions can vary from tiny water droplets dispersed in an oil phase (referred to as w/o microemulsion) to oil droplets dispersed in a water phase (o/w microemulsion), depending on the ratios of the components. The microstructure can change continuously, ranging from spherical to cylindrical, tubular, and interconnected continuous oil and water phases, separated by a thin layer of surfactant molecules (known as a discontinuous microemulsion).[4-8] All types of microemulsions are thermodynamically stable and appear transparent.

Emulsions, on the other hand, differ from microemulsions in terms of structure and stability. Emulsions are unstable systems that undergo phase separation without agitation. Additionally, the droplet size in emulsions typically ranges in the micrometer scale, while micelles in microemulsions have sizes in the range of 5-100 nm, depending on factors such as surfactant type, concentration, and degree of dispersion. It is worth noting that the term "microemulsion" can be misleading as it does not directly indicate the size of the dispersed phase droplets, which are actually in the nanometer range. The presence of electrolytes in the aqueous phase, along with the type of surfactants used, also influences the main characteristics of microemulsions.[9-10]

2. History:

The recognition of microemulsions began with the groundbreaking work of Hoar and Schulman in 1943. They observed the spontaneous

formation of an emulsion of water and oil upon the addition of a potent surface-active agent. The term "microemulsion" was coined by Schulman and his team in 1959 to describe a transparent solution consisting of water, oil, surfactant, and alcohol, forming a multiphase system. However, there has been ongoing debate regarding the use of the term "microemulsion" to describe such systems. While not universally adopted today, some prefer alternative names such as "micellar emulsion" or "swollen micelles" to refer to these systems.[11-13]

Microemulsions were likely discovered even before Schulman's studies. For instance, Australian housewives had been using mixtures of water, eucalyptus oil, soap flakes, and white spirit since the early 20th century to wash wool. Moreover, the liquid waxes discovered by Rodawald in 1928 are believed to be among the earliest examples of commercial microemulsions. However, it was in the late 1970s and early 1980s that interest in microemulsions gained significant traction.

Researchers recognized that these systems had the potential to enhance oil recovery, particularly as oil prices rose to levels where tertiary recovery methods became economically viable and profitable. Currently, the scope of microemulsion applications has expanded significantly beyond its conventional uses in detergents and lubrication. Around 60 additional applications have been identified, including catalysis, submicron particle preparation, solar energy conversions, and liquid-liquid extraction involving minerals and proteins. This broad range of applications continues to attract numerous scientists who are interested in exploring the potential of microemulsions.

Over the past two decades, there has been notable progress in understanding the fundamental characteristics of microemulsions from a scientific perspective. Advanced techniques such as small-angle neutron scattering, interfacial film stability measurements, and detailed structural analysis have contributed to significant advancements in the knowledge of microemulsions. These techniques

have enabled researchers to study the formation, stability, behavior, and gradient of phases within microemulsions in great detail.

In the following sections, we will delve into fundamental aspects of microemulsions, including their formation and stability, the characteristics of surfactant films, and the behavior and gradient of phases within these systems. This deeper understanding of microemulsion properties has paved the way for more precise control and utilization of these systems in various applications. [14-16]

3. Structure of Micro Emulsion

Microemulsions can be categorized into oil-in-water (o/w), water-in-oil (w/o), and bicontinuous microemulsions based on their structural organization. These microemulsions, also known as micellar emulsions, are dynamic systems where the interface between oil and water phases fluctuates spontaneously.

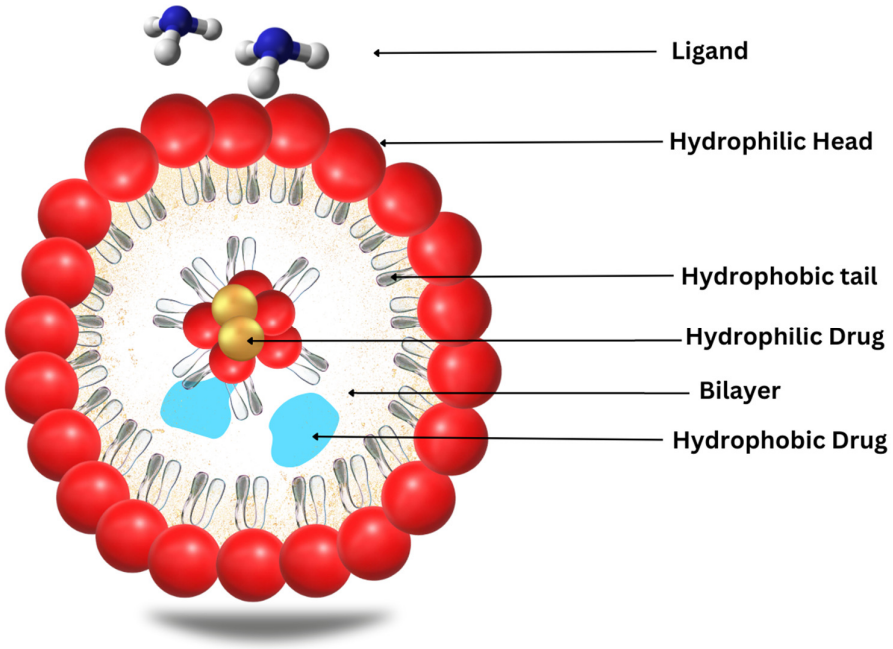

Fig.1: Structure of Microemulsion

In the case of oil-in-water (o/w) microemulsions, tiny water droplets are dispersed within the continuous oil phase. Conversely, in water-in-oil (w/o) microemulsions, small oil droplets are dispersed within the continuous aqueous phase. Bicontinuous microemulsions can

occur when the quantities of water and oil in the system are comparable.

The combination of oil, water, and surfactants can give rise to a wide range of phases and structures depending on the relative proportions of the components. These microemulsion systems exhibit constant and spontaneous fluctuations at the interface, which contribute to their dynamic behavior and unique properties.[17-21]

4. Characteristics

By utilizing a surfactant with balanced hydrophilic (water-loving) and lipophilic (oil-loving) properties at the appropriate concentration, it is possible to create a well-defined system of oil and water. This system, known as a "micro-emulsion," differs from traditional emulsions, such as milk emulsions, in several ways.

Micro-emulsions exhibit low viscosity and Newtonian flow characteristics, meaning their flow remains constant when subjected to various shear rates. In some cases, non-Newtonian flow and plasticity may be observed in discontinuous formulations. Even at high levels of dispersed droplets, the viscosity of micro-emulsions is similar to that of water. The interfacial tension between the phases and the energy required for droplet formation also play a role in the unique characteristics of micro-emulsions.[22-25]

The microstructure of microemulsions undergoes constant changes, resulting in highly dynamic systems where droplet coalescence is reversible. Various methods, such as light dispersion, X-ray diffraction, ultracentrifugation (UC), electrical conductivity, and viscosity tests, are employed to characterize the distinct properties of micro-emulsions.

These characterization techniques allow researchers to study factors such as droplet size, interfacial tension, flow behavior, and the stability of micro-emulsions. By understanding these characteristics, scientists can further explore the potential applications and optimize the performance of micro-emulsion systems.[25-27]

5. Classification of Micro Emulsion

According to Winsor, there are four equilibrium phases of microemulsions, which are commonly known as Winsor phases. These phases are:

1. Winsor I Phase (O/W Microemulsion): In this phase, the system consists of a large amount of oil, a small amount of water, and a surfactant. The microemulsion formed is oil-in-water (O/W), where oil droplets are dispersed within the continuous water phase.

2. Winsor II Phase (W/O Microemulsion): In this phase, the system contains a large amount of water, a small amount of oil, and a surfactant. The resulting microemulsion is water-in-oil (W/O), where water droplets are dispersed within the continuous oil phase.

3. Winsor III Phase (O/W/O Microemulsion): This phase involves a three-phase system with alternating layers of oil, water, and surfactant. The microemulsion has an oil-water-oil (O/W/O) structure, where water is trapped between two layers of oil.

4. Winsor IV Phase (W/O/W Microemulsion): This phase is also a three-phase system but with alternating layers of water, oil, and surfactant. The microemulsion exhibits a water-oil-water (W/O/W) structure, where oil is sandwiched between two layers of water.

These Winsor phases represent different equilibrium states that microemulsions can adopt, depending on the relative amounts of oil, water, and surfactant present in the system. Each phase has its own unique structure and characteristics, and understanding these phases is essential for studying the behavior and applications of microemulsions.

The R-ratio is one of the characteristics that Winsor initially introduced to describe the effect of amphiphiles (such as surfactants) and solvents on interface curvature. The R-ratio quantifies the relative affinity of an amphiphile for the oil phase compared to the water phase.

The R-ratio is calculated by dividing the concentration of the amphiphile in the oil phase by its concentration in the water phase. It provides insights into the preferential distribution of the amphiphile between the two phases and indicates whether the microemulsion formed will be oil-in-water (O/W) or water-in-oil (W/O).

If the R-ratio is less than one, it suggests that the amphiphile has a higher affinity for the water phase, favoring the formation of an O/W microemulsion. On the other hand, if the R-ratio is greater than one, it indicates a higher affinity for the oil phase, promoting the formation of a W/O microemulsion.[28-31]

6. Advantages of Microemulsion system:

1. Microemulsions are readily prepared without the need for energy due to their enhanced thermodynamic stability.

2. Microemulsions can undergo reversible formation. While they may become unstable at low or high temperatures, they readily reform into a microemulsion once the temperature stabilizes.

3. The thermodynamically stable nature of microemulsions allows for self-emulsification of the system.

4. Microemulsions exhibit low viscosity when compared to traditional emulsions.

5. Microemulsions possess exceptional solubility for medicinal compounds, enabling them to effectively dissolve both hydrophilic and lipophilic medications, including those that are insoluble in both hydrophobic and aqueous solvents.

6. Microemulsions have the ability to accommodate both lipophilic and hydrophilic pharmaceutical products.[32]

7. Disadvantages of Microemulsion Systems

1. Microemulsions have a limited capacity to solubilize high-melting substances.

2. Stabilizing droplets in microemulsions requires a significant amount of surfactants.

3. The stability of microemulsions is influenced by environmental factors such as temperature and pH.

8. INGREDIENTS OF MICROEMULSION

In the formulation and development of microemulsions, various substances are used. For a microemulsion to be suitable for biomedical and therapeutic applications, it is essential that the oils and surfactants employed are biocompatible, non-toxic, and therapeutically acceptable. The main components involved in microemulsion formulation are:

1. **Oil Phase:** The oil phase plays a vital role in microemulsions, especially when incorporating lipophilic medicinal products. It enables the solubilization of lipophilic drugs, allowing for effective delivery and improved absorption in the body, particularly through the lymphatic intestinal system. Oils used in microemulsions are typically liquids with low polarity and limited miscibility with water.

Examples of oils commonly employed in microemulsion formulations include cyclohexane, mineral oil, toluene, and vegetable oil. These oils provide a suitable medium for dissolving and carrying lipophilic medicinal products, ensuring their efficient dispersion and incorporation within the microemulsion system.

By utilizing an appropriate oil phase, microemulsions enhance the solubility and bioavailability of lipophilic drugs, facilitating their effective delivery and absorption in the body. The choice of oil depends on factors such as drug compatibility, desired properties of the microemulsion, and the targeted route of administration.

2. **Aqueous Phase:** The aqueous phase is composed of water and any additional water-soluble components or ingredients. It provides the aqueous environment required for the formation and stability of the microemulsion. The aqueous phase may also contain salts or other additives to adjust the properties of the microemulsion.

3. **Surfactant:** A surfactant, also known as a surface-active agent, is a chemical compound that exhibits interfacial or superficial activity, leading to a reduction in surface or interface tension. Surfactants have the unique property of being attracted to both polar and nonpolar liquids. These molecules consist of a polar head and a nonpolar tail, which give them their surfactant properties.

Surfactants play a crucial role in the formulation and development of microemulsions. They help to stabilize the system by reducing the interfacial tension between the oil and water phases, enabling the formation and maintenance of a stable microemulsion. Surfactant molecules have distinct intermolecular and intramolecular forces and are influenced by entropy considerations, which contribute to their independent behavior within the system.[33-38]

9. Types of surfactants

1**. Cationic surfactants**: These surfactants carry a positive charge on their polar head and are commonly used in applications such as antimicrobial agents and hair conditioners.

2. **Anionic surfactants**: These surfactants carry a negative charge on their polar head and are widely used in cleaning products, such as soaps and detergents.

3. Non-ionic surfactants: These surfactants do not carry an electrical charge and are often used in personal care products, pharmaceuticals, and food applications.

4. **Zwitterionic surfactants**: These surfactants contain both positive and negative charges within the same molecule, making them highly effective at reducing surface tension. They are commonly used in shampoos, skin cleansers, and other mild formulations.

The selection of surfactants depends on various factors, including their compatibility with the other components of the microemulsion, desired properties of the system, and the targeted application or formulation requirements.

4. **Co-solvent**: In some microemulsion formulations, a co-solvent is added to enhance the solubility of hydrophilic or lipophilic components. The co-solvent can help improve drug loading, enhance drug release, or optimize the properties of the microemulsion. Common co-solvents used in microemulsions include alcohols, glycols, and polyethylene glycols (PEGs).

Single chain surfactants alone may not be able to sufficiently decrease the interfacial tension between oil and water to produce a microemulsion in an oil-in-water (o/w) system. The addition of co-surfactants allows for more flexibility in achieving the necessary curvature to form a microemulsion with different excipients.

In cases where a single surfactant film is desired, the lipophilic chains of the surfactant should be either short enough or incorporate fluidization groups, such as unsaturated bonds. This helps in achieving the required fluidity and flexibility of the surfactant film, allowing it to effectively reduce the interfacial tension and promote the formation of a stable microemulsion.

The inclusion of co-surfactants in the formulation can help enhance the solubilization of both lipophilic and hydrophilic components, improve the stability of the microemulsion, and provide the necessary curvature to form and maintain the microemulsion structure. By combining different types of surfactants and co-surfactants, it is possible to optimize the interfacial properties and achieve the desired characteristics of the microemulsion formulation.

These components work together to create a stable and homogeneous microemulsion system. The selection of specific oils, surfactants, and co-solvents depends on the desired properties and intended applications of the microemulsion, ensuring biocompatibility and therapeutic acceptability.[39-45]

The preparation of a Microemulsion involves several steps, which are as follows:
1. Preparing the Water Phase: ● Dissolve water-soluble components in water. ● If there are solids, they can be dissolved by heating. ● Centrifuge the mixture to separate any undissolved material.
2. Preparing the Oil Phase: ● Dissolve oil-soluble components in the chosen oil phase.
3. Emulsifying the Water and Oil Phases: ● Mix the water phase and oil phase in a suitable vessel. ● Allow sufficient time for the two phases to equilibrate. ● Emulsification techniques such as stirring, using membranes, applying shear forces, or ultrasound can be employed to aid in the formation of the microemulsion.

By following these steps, the water-soluble and oil-soluble components are properly dissolved, and the emulsification process helps in achieving a stable and homogenous microemulsion. The selection of appropriate techniques and conditions for emulsification is crucial in obtaining the desired properties and stability of the microemulsion formulation.

10. Ternary Phase Diagram

A ternary phase diagram is a graphical representation of the phase behavior of a three-component microemulsion system under constant temperature and pressure. It consists of two or four distinct regions separated by demarcation lines.

Points located above the demarcation line in each region represent the composition of microemulsions within that particular phase area. These microemulsions exist as single-phase regions, meaning they have a uniform composition throughout.

The remaining areas in the phase diagram correspond to multiphase regions, which typically involve the coexistence of microemulsions with either an aqueous phase, an organic phase, or both. These systems fall under the classification of Winsor systems, where the presence of multiple phases is observed.

The ternary phase diagram provides valuable information about the composition and stability of microemulsion systems, helping researchers and formulators understand the phase behavior and optimize the formulation of microemulsions for various applications.[46-51]

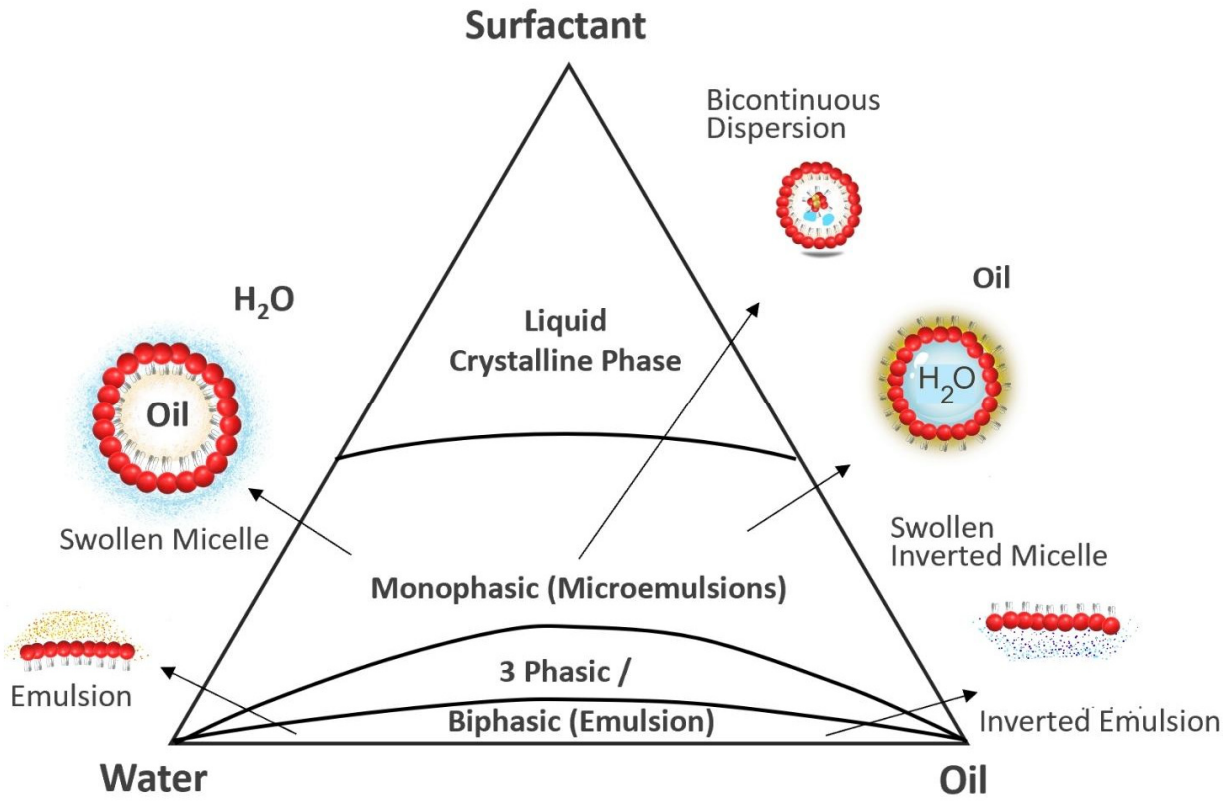

Fig.2 : Ternary Phase Diagram

11. Phases Involved in Microemulsion Systems:

1. Water Phase:

The water phase in a microemulsion system can serve two roles depending on its quantity. It can act as a dispersing medium, where water molecules surround and disperse the oil and surfactant components. Alternatively, if the water content is high, it can form a separate water pool within the microemulsion system.

2. Oil Phase:

The oil phase is a crucial component of microemulsions. The selection of the appropriate oil phase requires careful consideration. The choice of additional ingredients for the microemulsion formulation should align with the characteristics of the selected oil phase. Factors such as compatibility, stability, and desired properties of the final product must be taken into account when choosing the oil phase.[52-55]

12. Composition

The Major component in microemulsion system are

Component	Example
Oil:	1) Saturated fatty acids: Lauric acid, Capric acid 2) Unsaturated fatty acids: Oleic acid, Linoleic acid, Linolenic acid 3) Fatty acid esters: Ethyl or methyl ester of lauric acid, oleic acid, and myristic acid
Surfactant:	1) Polyoxyethylene/Polysorbate/Tween20,40,60,80 2) Sorbitan monolaurate, Egg lecithin 3) Sodium dodecyl sulfate
Co-surfactant:	1) Ethanol, Propanol, Butanol, Isopropanol, Pentanol, Hexanol 2) Polyoxyethylene-10-octyl ether 3) Sodium monohexyl phosphate 4) Cinnamic alcohol, Cinnamyl alcohol

13. Theories of Micro Emulsion Formation

1. **Interfacial or Mixed Film Theories:**

According to this theory, microemulsion formation occurs due to the formation of a mixed film at the oil-water interface. The surfactant molecules arrange themselves in such a way that their hydrophilic heads are in contact with water, while their hydrophobic tails are in contact with the oil phase. This arrangement reduces the surface tension at the interface and facilitates the formation of small droplets or micelles, which are dispersed throughout the system.

2. **Solubilization Theories:**

Solubilization theories propose that microemulsion formation involves the solubilization of oil or water phase within the surfactant micelles. The surfactant molecules form structures called reverse micelles, where the hydrophilic heads face inward and encapsulate the oil or water phase within their hydrophobic cores. This solubilization process allows for the formation of thermodynamically stable microemulsions.

3. **Thermodynamic Treatments:**

Thermodynamic treatments consider the free energy of microemulsion formation, which depends on the reduction in surface tension at the oil-water interface and the change in entropy of the system. The formation of microemulsion is favored when there is a large reduction in surface tension accompanied by a significant favorable entropic change. This favorable entropic change arises from processes such as the mixing of phases, surfactant diffusion in the interfacial layer, and surfactant exchange. Overall, the formation of microemulsion is considered spontaneous and thermodynamically stable when there is a negative free energy of formation.

The formation of a microemulsion is influenced by two factors: the reduction of surface tension at the oil-water interface by the surfactant and the change in entropy of the system. The free energy of microemulsion formation can be described in terms of these factors.

The surfactant plays a crucial role in lowering the surface tension between the oil and water phases. By reducing the surface tension, the surfactant promotes the formation and stability of the microemulsion.

Additionally, there is a change in entropy of the system during microemulsion formation. The mixing of the oil and water phases, in the form of numerous small droplets, contributes to a large dispersion entropy. Other dynamic processes, such as surfactant diffusion in the interfacial layer and monomer-micelle surfactant exchange, also contribute to favorable entropic changes.[56-61]

Taking these factors into account, the free energy of microemulsion formation is determined by the balance between the reduction in surface tension and the significant favorable entropic change. When there is a large reduction in surface tension accompanied by substantial entropic contributions, a negative free energy of formation is achieved. This indicates that the microemulsion formation is spontaneous and the resulting dispersion is thermodynamically stable.,

$$Gf = \gamma a - T S$$

Where,

Gf = free energy of formation
A = change in interfacial area of micro emulsion
S = change in entropy of the system
T = temperature
γ = surface tension of oil water interphase.

When a microemulsion is formed, there is a significant increase in interfacial area (A) due to the formation of a large number of very small droplets. In order for the formation of a transient microemulsion to occur, a negative change in A is required. However, it is recognized that although the value of A is positive at all times, it is very small and is offset by the entropic component.

The dominant favorable entropic contribution in microemulsion formation comes from the dispersion entropy generated by the mixing

of one phase into the other in the form of numerous small droplets. Additionally, there are other dynamic processes such as surfactant diffusion in the interfacial layer and monomer-micelle surfactant exchange that also contribute to favorable entropic changes.

In cases where there are significant reductions in surface tension accompanied by substantial favorable entropic changes, a negative free energy of formation is achieved. This indicates that the formation of the microemulsion is spontaneous, and the resulting dispersion is thermodynamically stable.[62-65]

14. Factor affecting Microemulsion

1.The packing ratio:

The hydrophilic-lipophilic balance (HLB) of the surfactant plays a role in determining the type of microemulsion by affecting the packing and curvature of the surfactant film.

2.Property of the surfactant:

Surfactants consist of hydrophilic and lipophilic groups. Surfactants with a hydrophilic single-chain, such as cetyl ammonium bromide, are fully dissociated in a dilute solution and tend to form oil-in-water (o/w) microemulsions.

3.Property of the oil phase:

The oil phase influences the curvature of the microemulsion by its capacity to penetrate and expand the tail group region of a surfactant monolayer. When the oil phase swells the tail region, it leads to enhanced negative curvature and the formation of water-in-oil (w/o) microemulsions.

4. Temperature:

The effective size of the head group of nonionic surfactants is crucial in determining the microemulsion behavior with temperature. At low temperatures, hydrophilic-oil-in-water (O/W) systems are formed, while at higher temperatures, lipophilic water-in-oil (W/O) systems are favored.[66-68]

15. APPLICATION OF MICROEMULSION SYSTEM

Microemulsion systems have found significant applications in the pharmaceutical industry over the past two decades. They offer several advantages in various pharmaceutical delivery methods:

a) *Parenteral Delivery*:
   Microemulsions are used for the administration of medicinal drugs with limited solubility, particularly through the intravenous route. Overcoming the challenge of delivering small amounts of medicine to a specific location is crucial in this context.

b) *Oral Delivery*:
   Microemulsion formulations provide several benefits compared to traditional oral formulations. These include improved absorption of drugs, enhanced clinical efficacy, and reduced drug toxicity.

c) *Topical Delivery*:
   The topical administration of medicines can be advantageous for several reasons. It helps in avoiding first-pass hepatic metabolism, degradation in saliva and stomach, and associated toxic effects.

d) *Ocular and Pulmonary Delivery*:
   In the treatment of eye disorders, drugs are often administered topically. O/W (oil-in-water) microemulsions have been explored for ocular delivery to dissolve poorly soluble drugs, improve drug absorption, and achieve a sustained release profile. The utilization of microemulsion systems in pharmaceuticals has opened up new possibilities for efficient drug delivery, addressing challenges related to solubility, absorption, and targeted administration.

e) *Nasal Delivery*:
   Microemulsions can be utilized for nasal drug delivery, enabling efficient absorption of drugs through the nasal mucosa and providing rapid systemic effects.

f) *Drug Targeting*:
Microemulsions can be designed to target specific sites in the body, allowing for controlled and localized drug delivery. This targeted approach enhances therapeutic outcomes and reduces systemic side effects.

g) Cellular Targeting:
By incorporating specific ligands or targeting moieties into the microemulsion formulation, it becomes possible to achieve cellular targeting. This facilitates the delivery of drugs directly to specific cells or tissues of interest.

h) *Brain Targeting*:
Microemulsions have shown promise in delivering drugs across the blood-brain barrier (BBB) for the treatment of various neurological conditions. They enhance the penetration of drugs into the brain, enabling effective therapy.

i) Periodontal Delivery:
Microemulsions can be employed for targeted delivery of drugs to the periodontal tissues, such as the gums. This approach allows for localized treatment of periodontal diseases and infections.

j) Tumor Targeting:
Microemulsion-based drug delivery systems can be designed for targeted delivery to tumors. They can improve drug accumulation in tumor tissues, enhance therapeutic efficacy, and minimize adverse effects on healthy tissues.

k) Microemulsion in Detergency:
Microemulsions have found applications in the field of detergency due to their ability to enhance the cleaning efficiency of various household and industrial cleaning products. The use of microemulsions in detergents allows for better dispersion of surfactants, oils, and other cleaning agents, resulting in improved soil removal and stain elimination. The small droplet size and enhanced stability of microemulsions contribute to their

effectiveness in removing dirt, grease, and other contaminants from surfaces. Furthermore, microemulsions can be formulated to be environmentally friendly, with reduced levels of harsh chemicals and improved biodegradability.

l) Microemulsion in Cosmetics:

In the cosmetics industry, microemulsions have gained attention for their ability to enhance the formulation and performance of various personal care products. Microemulsions can be used as delivery systems for active ingredients, allowing for improved penetration into the skin and enhanced efficacy. They can also provide a smooth and luxurious texture, improved stability, and prolonged release of cosmetic actives. Additionally, microemulsions can be tailored to different skin types, making them suitable for a wide range of cosmetic products such as lotions, creams, serums, and sunscreens.

m) Microemulsion in Food:

Microemulsions have emerged as valuable tools in the food industry due to their potential for enhancing product quality, stability, and functionality. They can be utilized for encapsulating flavors, colors, and bioactive compounds, protecting them from degradation and improving their solubility. Microemulsions can also improve the stability of emulsions, preventing phase separation and extending the shelf life of food products. Additionally, microemulsions can be used to reduce fat content in certain food formulations while maintaining desired sensory attributes. Their small droplet size and transparent appearance make them particularly suitable for clear and transparent food and beverage products.

The versatile nature of microemulsion systems makes them valuable in a wide range of pharmaceutical applications, offering enhanced drug delivery, targeting, and therapeutic outcomes.[69-75]

CONCLUSION

Microemulsions play a crucial role in both pharmaceutical drug delivery systems and industrial processes. They offer a means to optimize drug targeting while minimizing systemic absorption. Microemulsions provide new avenues for addressing challenges associated with poor water solubility and high bioavailability of highly lipophilic substances. However, there are still challenges to overcome, primarily related to the barriers that these systems must navigate to reach the intended target. Microemulsions can also be employed for drug targeting, protecting labile drugs, controlling drug release, and reducing patient variability. Overall, microemulsions offer promising opportunities for improving drug delivery and addressing various pharmaceutical needs.

References:

1. Vaibhav D. Mane*, Vipul M. Patil, Manisha V. Mane, Sachinkumar V. Patil. A review on microemulsion – a recent approach for topical drug delivery system. 2021 IJCRT | Volume 9, Issue 7 July 2021 | ISSN: 2320-2882
2. Ashwini Jadhav1*, Abhijeet Daundkar , Deepak Morale , Nikhil Bhujbal, Dr.Sandip Kshirsagar, Review on: Microemulsion a Novel Approach for Drug Delivery. Int. J. Pharm. Sci. Rev. Res., 52(2), September - October 2018; Article No. 11, Pages: 60-65 ISSN 0976 – 044X
3. Lachman L and Lieberman HA. The Theory and Practice of Industrial Pharmacy. 3rd Ed. Varghese Publishing house. 1990. pp. 534.
4. Vyas SP and Khar RK. Controlled Drug Delivery. 1st Ed. Vallabh Prakashan. 2002; 416-417.
5. B Prince, Leon M, Micro emulsions in Theory and Practice, Academic Press, New York, 1197.
6. Henri L, Clausse, Marc, Micro emulsion Systems, Marcel Dekker, 1987, 6.
7. Danielsson I, Lindeman, B, Colloids Surf. A 3, 1981, 391.
8. Sjoblom, J, Lindberg R,Friberg S. E, Adv. Colloid Interface Sci. 1996, 125.
9. Schulman J. H,Stoeckenius W,Prince M. J., Phys. Chem. 63, 1959, 1677.
10. Shinoda K,Friberg S,Adv. Colloid Interface Sci. 4, 1975, 281.
11. Lam AC, Schechter R S, The theory of diffusion in micro emulsions, J Colloid Interface Sci., 120, 1987, 56-63.
12. Hellweg T, Phase structure of micro emulsions, Curr opin colloid interface sci., 7, 2002, 50-56.
13. Maqsood A.M,Mohammad Y.W,Microemulsion method: A novel route to synthesize organic and inorganic nano materials, Arebian Journal of chemistry, 5(4), 2012, 397- 417.

14. Tenjarla S. Micro emulsions: an overview and pharmaceutical applications. Crit Rev Ther Drug Carrier Syst. 16(5), 1999, 461-521.
15. Lawrence MJ, Rees GD. Micro emulsion-based media as novel drug delivery systems. Adv Drug Deliv Rev. 45(1),
16. 2000, 89-121.
17. Vandamme TF. Micro emulsions as ocular drug delivery systems: recent developments and future challenges. Prog Retina Eye Res. 21(1), 2002, 15-34.
18. Bourrel, M,Schechter R. S, 'Micro emulsions and Related Systems' Marcel Dekker, New York, 1988.
19. Kumar. K. Senthil et al. Microemulsions as Carrier for Novel Drug Delivery: A Review. International Journal of Pharmaceutical Sciences Review and Research 2011; 10: 37-45.
20. Patel R. Mrunali. Microemulsions: As Novel Drug Delivery Vehicle. 2007; 5.
21. Madhav. S and Gupta. D. A review on microemulsion based system. 2011; 2 (8): 1888.Ghosh, P.K. and Murthy R.S.R. Microemulsions: A Potential Drug Delivery System. Current Drug Delivery 2006; 3: 167-180.
22. Chandra A. and Sharma P.K. Microemulsions: An Overview. Pharmainfonet 2008; 6 (2).
23. Patel M.R. et al. Microemulsions: As Novel Drug Delivery Vehicle. Pharmainfonet 2007; 5(6)
24. Kayes F. B. Disperse systems In Pharmaceutics: The Science of Dosage Form Design. International Student Edition Ed: Aulton. M.E. Churchill Livingstone 1999; 110.
25. Emsap. W.J. et al. Disperse Systems in Modern Pharmaceutics. Fourth Edition. Ed: Banker. G.S. Rhodes, C.T. Marcel Dekker Inc. New York. 2002; p260.
26. Sarkhejiya Naimish A et al. Emerging Trend of Microemulsion in Formulation and Research. International Bulletin of Drug Research. 2000; 1 (1): 54-83.

27. Jha Sajal Kumar et al. Microemulsions- Potential Carrier for Improved Drug Delivery. International Pharmaceutica Sciencia 2011; 1(2): 25-31.
28. Vyas S P. Theory and practice in novel drug delivery system. CBS Publishers New delhi. 2009; p115.
29. Prince L. M. A theory of aqueous emulsions I. Negative interfacial tension at the oil/water interface. Journal of colloid and interface science 1976;23:165-173.
30. MartinA. Coarse dispersions in physical Pharmacy. Fourth Edition B.I. Waverly Pvt. Ltd. New Delhi. 1994; 495.
31. Rao Y.S. et al. Microemulsions: A Novel Drug Carrier System. International Journal of Drug Delivery Technology 2009; 1(2): 39-41.
32. Grampurohit N. et al. Microemulsions for Topical Use- A Review. Indian journal of Pharmaceutical Education and Research. 2011;45(1):100-107.
33. Ashwini Jadhav, Abhijeet Daundkar, Deepak Morale, Nikhil Bhujbal, Dr.Sandip Kshirsagar. Review on: Microemulsion a Novel Approach for Drug Delivery. International Journal of Pharmaceutical Sciences Review and Research. 52(2) : 2018; 60-65.
34. Khan AY, Talegaonkar S, Iqbal Z, Ahmed FJ, Khar RK. Multiple emulsions: an overview. Current Drug Delivery. 3(4), 2006, 429-43.
35. Kumar P, Mittal KL. Handbook of Micro emulsion Science and Technology; 1st Edition; CRC Press, New York, 1999.
36. Tang JL, Sun J, He ZG. Self-Emulsifying Drug Delivery Systems: Strategy for Improving Oral Delivery of Poorly Soluble Drugs. Current Drug Therapy. 2(1), 2007, 85-93.
37. Talegaonkar S, Azeem A, Ahmad FJ, Khar RK, Pathan SA, Khan ZI. Micro emulsions: A Novel Approach to Enhanced Drug Delivery. Recent Patents on Drug Delivery & Formulation. 2(3), 2008, 238-257.

38. Min DI. ,Neoral: a micro emulsion cyclosporine. J Transpl Cord Review. Erratum in: J Transpl Coord. 6(2), 1996, 52.
39. Lawrence MJ, Rees GD. Micro emulsion-based media as novel drug delivery systems. Adv Drug Deliv Rev. 45(1), 2000, 89-121.
40. Flanagan J, Singh H. Micro emulsions: a potential delivery system for bioactives in food. Crit Rev Food Sci Nutr. 46(3), 2006, 221-37.
41. Ghosh PK, Murthy RS. Micro emulsions: a potential drug delivery system. Curr Drug Deliv. 3(2), 2006; 167-80. 22.
42. Jadhav KR, Shaikh IM, Ambade KW, Kadam VJ. Applications of micro emulsion based drug delivery system. Curr Drug Deliv, 3(3), 2006, 267-73.
43. Talegaonkar S, Adnan Azeem, Farhan Ahmad J, Roop Khar K, ; Micro emulsions: A Novel approach to enhanced drug delivery; Recent patents on drug delivery and formulation; 2, 2008, 238-257.
44. Ramadan, r., Devarajan, p.v.; Micro emulsion Indian Drugs, 2003, pg.no:139-146.
45. Shaji, J., Reddy, M.S.; Micro emulsion as drug delivery system, Parma Times, 2004, 139-146.
46. The Theory and practices of Industrial pharmacy, Leon Lacham, Herbert a. Liberman special Indian edition 2009, 507-530.
47. Ashok Patel and Pradeepvavia R. Preparation and In-vivo Evaluation of Self-Microemulsifying Drug Delivery System Containing fenofibrate. The AAPS Journal 2007; 226: 344-352
48. Peltola S. et al. Microemulsions for topical delivery of estradiol. International Journal of Pharmaceutics 2003; 254: 99-107.
49. Hsiu-O Ho. et al. Preparation of microemulsions using polyglycerol fatty acid esters as surfactant for the delivery of protein drugs. Journal of Pharmaceutical Sciences 1996; 85: 138-143.

50. Corswant C. et al. Triglyceride –based microemulsion for intravenous administration of sparingly soluble substances. Journal of Pharmaceutical Sciences 1998; 87: 200-208.
51. Dreher F. et. al. Interaction of a lecithin microemulsion gel with human stratum corneumand its effect on transdermal transport. Journal of Controlled Release 1997; 45:131 140.
52. Lv FF. et al. Studies on the stability of the chloramphenicol in the microemulsion free of alcohols. European Journal of Pharmaceutics and Biopharmaeutics 2006; 62: 288-294.
53. Syamasri Gupta and S.P. Moulik. Biocompatible microemulsions and their prospective uses in drug delivery. Journal of Pharmaceutical Sciences. 2008; 97: 22-45.
54. Shiokawa T. et al. Effect of Polyethylene Glycol Linker Chain Length of Folate-Linked Microemulsions Loading Aclacinomycin A on Targeting Ability and Antitumor Effect In itro and In vivo. Clinical Cancer Research 2005; p11.
55. Talegaonkar S and Mishra P. Intranasal delivery: An approach to bypass the blood brain barrier. Indian Journal of Pharmacology 2004; 36: 140-147.
56. Hasse. A. and Keipert S. Development and characterisation of microemulsions for ocular application. European Journal of Pharmaceutics and Biopharmaeutics 1997; 43; 179–183.
57. Tenjarla S. Micro emulsions: an overview and pharmaceutical applications. Crit Rev Ther Drug Carrier Syst.16(5), 1999, 461-521.
58. Lawrence MJ, Rees GD. Micro emulsion-based media as novel drug delivery systems. Adv Drug Deliv Rev. 45(1), 2000, 89-121.
59. Vandamme TF. Micro emulsions as ocular drug delivery systems: recent developments and future challenges. Prog Retina Eye Res. 21(1), 2002, 15-34.
60. Bourrel, M,Schechter R. S, ‘Micro emulsions and Related Systems’ Marcel Dekker, New York, 1988.

61. Khan AY, Talegaonkar S, Iqbal Z, Ahmed FJ, Khar RK. Multiple emulsions: an overview. Current Drug Delivery.3(4), 2006, 429-43.
62. Kumar P, Mittal KL. Handbook of Micro emulsion Science and Technology; 1st Edition; CRC Press, New York, 1999.Tang JL, Sun J, He ZG.
63. Self-Emulsifying Drug Delivery Systems: Strategy for Improving Oral Delivery of Poorly Soluble Drugs. Current Drug Therapy. 2(1), 2007, 85-93.
64. Talegaonkar S, Azeem A, Ahmad FJ, Khar RK, Pathan SA, Khan ZI. Micro emulsions: A Novel Approach to Enhanced Drug Delivery. Recent Patents on Drug Delivery & Formulation. 2(3), 2008, 238-257.
65. Min DI. ,Neoral: a micro emulsion cyclosporine. J Transpl Cord Review. Erratum in: J Transpl Coord. 6(2), 1996, 52.
66. Lawrence MJ, Rees GD. Micro emulsion-based media as novel drug delivery systems. Adv Drug Deliv Rev. 45(1), 2000, 89-121.
67. Flanagan J, Singh H. Micro emulsions: a potential delivery system for bioactives in food. Crit Rev Food Sci Nutr. 46(3), 2006, 221-37.
68. Ghosh PK, Murthy RS. Micro emulsions: a potential drug delivery system. Curr Drug Deliv. 3(2), 2006; 167-80.
69. Jadhav KR, Shaikh IM, Ambade KW, Kadam VJ. Applications of micro emulsion based drug delivery system. Curr Drug Deliv, 3(3), 2006, 267-73.
70. Talegaonkar S, Adnan Azeem, Farhan Ahmad J, Roop Khar K, ; Micro emulsions: A Novel approach to enhanced drug delivery; Recent patents on drug delivery and formulation; 2, 2008, 238-257.
71. Shafiq un Nabi S, Shakeel F, Talegaonkar S; Formulation development and optimization using nanoemulsion technique: A technical note; AAPS Pharm Sci Tech., 8, 2007, 1-6

72. Jha Sajal Kumar, Dey Sanjay, Karki Roopa, Micro emulsions Potential Carrier for Improved Drug Delivery, International Pharmaceutical Science., 1(2), 2011, 25-31.
73. Vyas S P; Theory and practice in novel drug delivery system; CBS Publishers, New Delhi, 1, 2009, 115-116. 27. Prince L. M; A theory of aqueous emulsions I. Negative interfacial tension at the oil/water interface; J. Colloid Interface Sci., 23, 1976, 165-173.
74. Ramadan, r., Devarajan, p.v.; Micro emulsion Indian Drugs, 2003, pg.no:139-146. 29. Shaji, J., Reddy, M.S.; Micro emulsion as drug delivery system, Parma Times, 2004, 139-146.
75. The Theory and practices of Industrial pharmacy, Leon Lacham, Herbert a. Liberman special Indian edition 2009, 507-530.