IJBPAS, September, 2023, 12(9): 3962-3970

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

MICROEMULSIONS: A BRIEF OUTLOOK

JAIN D[1*], TADVI S[2], DHANKANI A[3], PATEL N[4] AND PAWAR S[5]

[1-5]Department of Pharmaceutics, P.S.G.V.P.M'S College of Pharmacy, Shahada-425409, Maharashtra, India

[*]**Corresponding Author: Mr. Darshan D Jain: E Mail: darshanjain.dj57@gmail.com**

Received 25th June 2022; Revised 18th Aug. 2022; Accepted 11th Dec. 2022; Available online 1st Sept. 2023

https://doi.org/10.31032/IJBPAS/2023/12.9.7329

ABSTRACT

Transparent, stable, isotropic concoctions of oil, water, and a surfactant often in conjunction with a cosurfactant are recognized as microemulsions. The melioration of bio-availability of drugs is one of the greatest challenges in drug formulations. In comparison to many other approaches, microemulsions has bagged superfluous attention due to their ameliorated oral bio availability, extended shelf life, simplicity in preparation and administration, and thermodynamic stability. Microemulsions are amidst the significant options as innovative drug delivery systems. This review sets out to discuss types, merits, demerits, components, methods of preparation, factors affecting formulation and evaluation parameters of microemulsions.

Keywords: Microemulsion. Phase Diagram, Surfactant, Co-surfactant, Bioavailability

INTRODUCTION:

Pharmaceutical research is always attempting to develop new drug delivery systems that will increase the potency of already available medications. Since there are several drug delivery systems that have been developed. Hoar and Schulman formulated a transparent single-phase solution by triturating a milky emulsion with hexanol in 1940, introducing the idea of the microemulsion. By dispersing oil in an aqueous surfactant solution and adding alcohol as a co-surfactant, they created the first microemulsion, resulting in a clear, stable formulation **[1]**.

Microemulsions are transparent, stable, isotropic concoctions of oil, water, and a surfactant often in conjunction with a cosurfactant. The typical range for droplet

size is between 10-100 nm. These homogeneous systems are all low viscosity fluids that may be created with a variety of surfactant concentrations and oil to water ratios. Additionally, the tiny droplets offer improved membrane adhesion and controllable drug molecule delivery. Moreover, due to size reduction, it provides a bigger surface area, which eventually increases absorption and thereby ameliorate bioavailability. These systems give a lot of benefits for oral administration **[2, 3, 4]**.

Types of Microemulsions: [5]

Winsor identified four different types of micro emulsion phases that are present in equilibrium and are referred to as Winsor phases. As follows:

Winsor I (two phase system):

Top oil layer and bottom (o/w) micro emulsion phase are in equilibrium. It is also called as Type-I microemulsion.

Winsor II (two phase system):

The upper (w/o) micro emulsion and lower surplus water are in equilibrium. . It is also called as Type-II microemulsion.

Winsor III (three phase system):

Upper phase oil and lower phase water are in equilibrium with the intermediate bi-continuous phase of o/w and w/o. It is also called as Type-III microemulsion.

Winsor IV (single phase system):

It generates homogenous concoction of oil, water and surfactant. It is also called as Type-1V microemulsion.

Merits: [6, 7]

- Easy preparation due to better thermodynamic stability.
- Ability to carry both lipophilic and hydrophilic drugs.
- Boost a drug's effectiveness, enabling the total dose to be reduced and thus minimizing side effects.
- The small size of droplet in microemulsions yields very large interfacial area, from which the drug is released rapidly into external phase when absorption takes place, maintaining the concentration in the external phase close to initial levels.

Demerits: [8, 9]

- Microemulsion stability is influenced by environmental parameters such as temperature and pH.
- Limited solubilizing capacity for high-melting substances used in the system.
- Require large amount of Surfactants for stabilizing droplets.

Compositions of Microemulsion:

Oil Phase:

Any liquid with low polarity and poor miscibility with water is considered oil. These phases include toluene, cyclohexane, mineral oil, and vegetable oil, for instance. **[7]**

Aqueous phase:

Preservatives and hydrophilic active ingredients often develop in the aqueous phase. As an aqueous phase, buffer solutions are used occasionally **[10]**.

Surfactant:

Surfactant, also known as a surface-active agent, refers to a chemical that has some interfacial or superficial activity and is used to lower surface or interface tension. Polar and nonpolar liquids both capture its attention. Surfactants are molecules with a polar head and a polar tail. Because of various intramolecular and intermolecular forces, as well as entropy considerations, surfactant molecules are independent **[10]**.

The several surfactants included in the technique of progressive microemulsion development includes:

1. Cationic

2. Anionic

3. Non-ionic

4. Zwitterionic surfactants.

Co-surfactant

A microemulsion cannot be formed by single-chain surfactants because they are unable to lower the o/w interfacial tension significantly. The addition of co-surfactants enables the interfacial film to be flexible to take up different curvatures required to form microemulsion across a variety of excipients. If a single surfactant film is needed the lipophilic chains of the surfactant should be suitably short or contain fluidizing groups (e.g. unsaturated bonds). Basic co-surfactants are short chain alcohols (ethanol to butanol), glycols such as propylene glycol, medium chain alcohols, amines or acids. Co-surfactants are used to dissolve any liquid crystal or gel formations that have formed instead of the microemulsion phase **[11]**.

Method of Preparation: [12, 13, 14]

We can formulate microemulsion primarily using two methods, which are as follows:

Phase Titration Method:

The phase titration technique is used to make microemulsions. These are also referred to as the spontaneous emulsification technique. Microemulsions can be characterized by the phase diagram. As four compartment systems are time-consuming and complex to intercept Therefore, we use the pseudo ternary phase diagram in the preparation of microemulsions. These have several zones, including microemulsion zones. We use predetermined weight ratios of oils, water, surfactants, and a combination of co-surfactants in our phase titration approach. The mixing of the materials is accomplished via this phase diagram. All of these mixes will be agitated at room temperature, and the presence of a monophasic or biphasic system will then be determined visually. In phase separation turbidity might emerge, the samples should be thought of as biphasic since, following

continued stirring, monophasic mixtures look clear and transparent. The phase diagram has to be marked with the acquired points.

Phase Inversion Method

Microemulsions undergo phase inversion when too much of the dispersed phase is added or when the temperature changes. Physical changes in particle size can happen during the phase inversion procedure, which can eventually alter both the in-vitro and in-vivo release of drugs. For non-ionic surfactants can be achieved by altering the system's temperature. In these procedures, an o/w microemulsion turns into a w/o microemulsion at low temperatures. This is also referred as transitional phase inversion method. As the system cools, it crosses the spontaneous zero-point shape, maintains surface tension, and intensifies the formation of oil droplet dispersion. In addition to temperature, salt content and pH level may be taken into account. In this phase inversion method, the water volume fraction can change, causing a transition in the radius. By adding water to oil, water droplets are first generated in a continuous oil phase. By employing temperature to stabilise surfactants from stabilising a w/o microemulsion to an o/w microemulsion, water volume fraction may be enhanced.

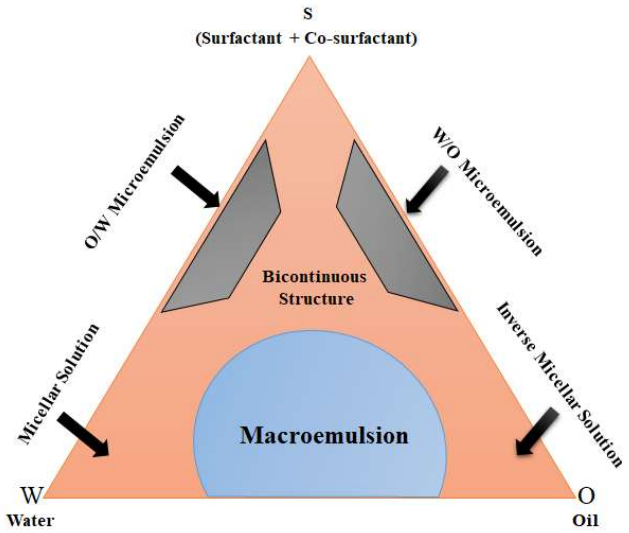

Figure 1: Pseudoternary Phase Diagram

FACTORS AFFECTING MICROEMULSION FORMATION: [15, 4]

Packing Ratio:

The type of microemulsion is determined by the surfactant's HLB through its impact on packing and film curvature. The examination of film curvature for surfactant

interactions enabling microemulsion to develop.

$$\textbf{Critical packing ratio} = \frac{V}{a \times l}$$

Where,

V = volume of surfactant molecule

a =head group surface area

l = length

If CPP is between 0-1, interface curves towards water (positive)

If CPP $>$ 1, interface curves towards oil (negative)

If CPP $=$ 1, then either bicontinuous or lamellar structure

Role of Surfactant:

Two groups of hydrophilic and lipophilic molecules make up surfactant. Hydrophilic single chain surfactants such as cetylethylammonium bromide dissociate completely in dilute solution and has a propensity to form o/w microemulsion. When a surfactant is applied at a high concentration or when salt is present, the degree of polar group dissociation is reduced, and the resultant system may be w/o type.

Property of Oil Phase:

Oil phase also influence curvature by its ability to penetrate & Swell the tail group region of the surfactant monolayer, swelling of tail results into an enhanced negative curvature to w/o microemulsion.

Temperature:

The size of the non-ionic surfactant's effective head group is significantly influenced by temperature. At low temperature, they are hydrophilic & form normal o/w microemulsion whereas at high temperature, they are lipophilic & form normal w/o microemulsion and at an intermediate temperature, microemulsion coexist with surplus water and oil phase and form bicontinuous structure.

Chain length, Type and nature of cosurfactant:

Shorter chain cosurfactant addition has a favourable curvature effect because alcohol expands the head area more than the tail region, making it more hydrophilic and favouring the o/w type. Alcohol swelling favours w/o type by swelling more in the tail than the head when longer chain cosurfactant is added.

EVALUATION PARAMETERS OF MICROEMULSION:

1] Physical appearance:

For physical appearance microemulsion can be inspect visually for homogeneity, fluidity and optical clarity **[16]**.

2] Identification of type of emulsion:

a) Drop dilution test:

The dilutions were prepared as follows: 1 ml of microemulsion in 10 ml, 1 ml of microemulsion in 100 ml, and 1 ml of microemulsion in 1000 ml of distilled water **[18]**.

b) Dye solubility test:

Add the prepared microemulsion to the water soluble dye (Amaranth) and examine for uniform distribution of dye within microemulsion. **[18]**

3] Emulsifying Time:

The emulsifying time of that particular microemulsion formulation was defined as time it took for the microemulsion to emulsify in water and get miscible in it. Pour 1ml of the microemulsion formulation into some water, and notice how long it takes to emulsify. **[17]**

4] pH:

The pH of formulated microemulsions were measured using a digital glass electrode pH-meter. The pH meter was first calibrated using solution of pH 7 buffer solution **[18]**.

5] Viscosity:

Viscosity of the formulated microemulsions were determined by using digital viscometer (Fungi lab). Viscosity was measured at 10 rpm for 30 seconds for microemulsion formulation by using L-2 spindle **[19]**.

6] Electron Microscope Characterization:

The most crucial method for examining the microstructures of microemulsions is transmission electron microscopy (TEM), which can record any co-existing structure as well as micro structural transformations and instantly generates high-resolution pictures.

TEM are two versions of the TEM method for fluid samples i.e, Cryo-TEM (samples are directly observed after quick freezing and freezing fructose in the cold microscope) and Freeze Fracture (a replica of the specimen is images under RT conditions) **[20]**.

7] Drug content:

The drug content of each preparation is measured by diluting 1 ml of the formulation to 100 ml with an appropriate solvent and shaking intensely. 1 ml was remove from the solution and then diluted to 25 ml with the same solvent. The absorbance of the solution was determined spectrophotometrically at a specific wavelength. The drug content (%) was calculated by use of given equation: **[21]**

$$\textit{Drug content}\ (\%) = \frac{\textit{Drug concentration}\ (\textit{sample solution}) \times 100}{\textit{Equivalent concentration}\ (\textit{drug taken})}$$

8] Diffusion study:

Diffusion studies for each formulation were performed using Franz diffusion cells. An egg membrane was used as the diffusion membrane. The membrane was saturated in a 0.1N HCl solution for 24 Hrs before the experiment. The receptor chamber was filled with the 0.1N HCl solution and the membrane was placed over the cell. The microemulsion corresponding to 25 mg of drug was placed in the donor chamber. It was in contact with receptor compartment

containing 0.1N HCl solution. The cell was agitated by a magnetic stirrer at 50 rpm and temperature was maintained at 32-34 °C using a circulating water bath. Aliquots were withdrawn at specific time intervals till 7 hrs and refilled with an equal amount of fresh 0.1N HCl solutions to maintain sink condition, filtered, and finally the absorbance of the drug was determined spectrophotometrically at 237 nm **[22]**.

CONCLUSION:

From this article we concluded that in recent years microemulsions have very pivotal importance in the novel drug delivery system. Microemulsions are commercially easy and appropriate vehicle for delivery of medicaments which provides new solution to overcome problems associated with drug having poor aqueous solubility. It enhance drug absorption by enhancing its aqueous solubility which helps to ameliorate bioavailability of poorly water soluble drug with reduced systemic side effects. It is intimately proposed that this review will guide to comprehend and further to advance the microemulsion based dosage forms to acquire certain medicinal goals.

REFERENCES:

[1] Hoar TP, Schulman JH. Transparent water-in-oil dispersions, the oleopathic hydro micelle. Nature.,152, 1943, 102–103

[2] Danielsson I, Lindman B. The definition of a microemulsion. Colloids and Surfaces,, 3, 1981, 391–392

[3] Sarkhejiya NA, Nakum MA, Patel VP, Atara SA, Desai TR. Emerging trend of the microemulsion in formulation and research. Int Bull Drug Res., 1, 2010, 54-83

[4] Lawrencea MJ, Rees GD. Microemulsion-based media as novel drug delivery systems. Advanced Drug Delivery Reviews., 45, 2000, 89–121

[5] Mane VD, Patil VP, Mane MV, Patil SV. A Review on Microemulsion – A Recent Approach for Topical Drug Delivery System. International Journal of Creative Research Thoughts., 9(7), 2021, c62-c71

[6] Kumar KS *et al*. Microemulsions as Carrier for Novel Drug Delivery: A Review. International Journal of Pharmaceutical Sciences Review and Research., 10, 2011, 37-45

[7] Madhav S and Gupta D. A review on microemulsion based system. International Journal of Pharmaceutical Sciences and Research., 2(8), 2011, 1888

[8] Ghosh PK, Murthy RS. Microemulsions: A Potential Drug

Delivery System. Current Drug Delivery., 3, 2006, 167-180

[9] Chandra A, Sharma PK. Microemulsions: An Overview. Pharma info net., 6(2), 2008

[10] Rao YS *et al*. Microemulsions: A Novel Drug Carrier System. International Journal of Drug Delivery Technology., 1(2), 2009, 39-41

[11] Grampurohit N *et al*. Microemulsions for Topical Use-A Review. Indian Journal of Pharmaceutical Education and Research., 45(1), 2011, 100-107

[12] Patel MR, Patel RB, Parikh JR, Bhatt KK, Kundawala AJ. Microemulsions: As Novel Drug Delivery Vehicle, Pharmainfonet., 5, 2007, 6

[13] Agrawal OP, Agrawal S. An Overview of New Drug Delivery System: Microemulsion. Asian J. Pharm. Sci. Tech., 2(1), 2005, 5-12

[14] Bysu S, Himabindu E , Sowjanya B ,Konde A. Microemulsions-A review. J. Pharm. Sci. & Res., 12(6), 2020, 750-753

[15] Lawrence MJ. Surfactant systems: microemulsions and vesicles as vehicles for drug delivery. Eur. J. Drug Metab. Pharmacokinet., 19(3), 1994, 257–269

[16] Singh PK, Mohammad IK, Shukla VK, Mohd S. (2014). Review Article Microemulsions: Current Trends in Novel Drug Delivery Systems., 1, 2014, 39-51

[17] Khoo SM, Andrew JH. Formulation design and bioavailability assessment of lipidic self-emulsifying formulations of halofantrine. Int J Pharm., 167, 1998, 155-164

[18] Prince LM. A theory of aqueous emulsion. I. Negative interfacial tension at the oil/water interface. J. Colloid Interface Sci., 23, 1967, 165–173

[19] Patel TB, Patel TR, Suhagia BN. Preparation, characterization, and optimization of microemulsion for topical delivery of itraconazole. Journal of Drug Delivery and Therapeutics., 8(2), 2018, 136-145

[20] Sharma N, Antil V, Jain S. MICROEMULSION: A REVIEW. Asian Journal of Pharmaceutical Research and Development., 1(2), 2013, 23-26

[21] Khoo SM, Humberstone AJ, porter CJH, Edwards GA, Charman WN. Formulation Design and Bioavailability Assesment of Lipidic Self-Emulsifying Formulations of Halofantrine. International Journal of

Pharmaceutics.,167, 1998, 155-164

[22] Giustini M. *et al*. Microstructure and dynamics of the water-in-oil CTAB/n-pentanol/nhexane/water microemulsion: spectroscopic and conductivity study. Journal Physical Chemistry., 100, 1996, 3190 3198.