



Review Article

A REVIEW ON MICROEMULSION A PROMISING OPTIMISING TECHNIQUE USED AS A NOVEL DRUG DELIVERY SYSTEM

Anurag Chaudhary, Moumita Barman *, Praveen Kumar Gaur, Rosaline Mishra, Monika Singh
I.T.S. College of Pharmacy, Ghaziabad, India

*Corresponding Author Email: moumitabarman@its.edu.in

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ABSTRACT

Micro-emulsions are unit optically and macroscopically isotropous mixtures of a minimum of a hydrophilic associated, a hydrophobic and an amphiphilic half. These are unit stable than different emulsion forms, clear, usually conjoint with a co surfactant their diameter is within the parameter of 10-140µm. These days, the micro-emulsion formulations are unit accepted everywhere to deliver the hydrophilic yet because the lipophilic medications as drug carriers as a result they need lots of additional wonderful drug solubilizing ability, long time period, better bioavailability, the comfort of preparations, ultra-low surface tension and enormous surface space. During this critical review, the varied benefits, disadvantages, limitations, of micro-emulsions within the prescription drugs, ways of preparation, types of micro-emulsion, analysis parameters and therefore the totally different analysis works on the micro-emulsions squares measure represented.

Keywords: Microemulsions, hydrophilic, lipophilic, hydrophobic, pharmaceutical, bioavailability.

INTRODUCTION

The concept of Micro-emulsions stayed not really documented while waiting for the work of Hoar and Schulman in 1943, who described a impulsive emulsion of oil and water on adding of a durable surface-active agent. The term “micro-emulsion” was 1st used even later by Schulman et al. in 1959 to explain a point system consisting of alcohol oil water and surfactants that forms a clear solution. There has been a lot of dialogue the word “micro-emulsion” to explain such systems though not consistently used nowadays, some like the names “micellar emulsion” or “swollen micelles”.¹ The most excellent definitions of microemulsions is “a micro-emulsion may be a system of oil, water also an amphiphile that may be a single optically identical and thermodynamically stable liquid solution”.

It is well acknowledged that enormous amounts of 2 incompatible liquids (e.g. oil and water) are often conduct into a distinguished phase (microscopically heterogeneous however macroscopically homogeneous) by addition of a well-suited surface-active-agent or a surface-active-agent mixture. These exclusive class of optically clear, thermodynamically stable and commonly low viscous solutions, known as ‘micro-emulsions’.² Micro-emulsions are unit clear, homogenous, thermo-dynamically stable dispersions of oil and water that area typically stable by a surface-active-agent, preferably together to a surface-active-agent and their general drop diameter lies within the vary of within 10-140µm.³ This system is satisfactory for delivery of both water unsolvable drugs and water solvable drugs. Water un-soluble medicines also delivered through oil-in-water (o/w) micro-emulsions, whereas water solvable drug may be delivered through water-in-oil (w/o) micro-emulsions⁴

Macroscopically, micro-emulsions square measure identical mixtures of at the most a hydrophilic, a hydrophobic associate and

an amphiphilic element. Their natural philosophy stability and their nanostructure square measure 2necessary distinctive that discriminate them from normal emulsion that square measure thermo-dynamically unstable.⁵ as the area of the elements is far shorter than the wave-length of observable light (400–800 nm), micro-emulsions are crystal-clear and their construction can’t be detected through associated degree optical magnifier. As a result, micro-emulsions arise as clear solutions and are a lot of satisfactory physically as compared to ordinary-emulsions.⁶

Difference between micro-emulsions and emulsions

The greatest difference between micro-emulsions and emulsions exist within the form and size of the elements that are propagate within the constant phase is a general way these are a demand of magnitude shorter within the circumstance of micro-emulsions (10-200nm) than individuals of ordinary emulsions (1-20µm). One more main difference fascinates their presence; micro-emulsions squad measure clear or lustrous whereas emulsions square measure cloudy. In accumulation, there square measure distinct variations in their methodology of preparation, since emulsions need an oversized input of energy whereas micro-emulsions don’t.⁷

TYPES OF MICRO-EMULSION⁸

- There square measure four sorts of micro-emulsion segments conferring by Winsor exists in equilibrium, these segments are discussed, they are:
- Two phase system (Winsor 1): upper oil layer exists in equilibrium with lower (o/w) micro emulsion phase
- Two phase system (Winsor 2): the upper (w/o) micro emulsion exists within equilibrium with lesser spare water.

- Three phase system (Winsor 3): mid bi-continuous stage of oil/water and water/oil called) exists in equilibrium with greater phase oil and lesser phase water.
- Single phase system (Winsor 4): it forms homogenous mixture of surface-active-agent, oil and water.
- R-ratio remains one in every of the depiction not ions that remain initial anticipated through Winsor to explicate the impact of amphiphiles and diluents on surface curvature. The R-ratio relates the empathy for associate degree amphiphile in the direction of dissolved obsessed by oil, near its empathy on the way to liquefy in water. If one section is preferred, the surface region forms a certain curvature. Hence, If $R > One$, the interface will increase its space of interaction by oil whereas reducing its space of interaction with water. Consequently, oil converts in the constant stage in addition the equivalent representative system is sort2 (Winsor 2). In the same way, a well-adjusted Interfacial film is denoted by $R = One$.

Advantages⁹⁻¹¹

Thermodynamically constancy and need tiniest energy for development.

- To solubilize hydrophobic or oil soluble drugs
- Improved medication solubilization and enhanced bioavailability.
- Micro-emulsion is unit consuming varied submissions in mixture drug delivery systems for the aim of drug aiming and controlled release.
- Micro-emulsion can be utilized for oral, parenteral, and topical drug delivery.
- Taste masking of unpleasant drugs can be done with the help of micro emulsion
- To improve palatability of nutrient oils.

Disadvantages¹²⁻¹⁴

- Consuming incomplete solubilizing volume for high melting ingredients.
- Necessitate huge quantity of Surface-active-agent used for all evirating droplets.
- Micro-emulsion constancy is prejudiced via conservational structures such as temperature and hydrogen ion concentration.

Limitations of the micro-emulsion system¹⁵⁻¹⁷

There are certain reasons which limit the utilization of the micro-emulsion systems within the medicinal submissions:

- There is a common problem of phase separation seen in the case of micro-emulsions.
- For toxicity reasons, the concentrations of the co-surfactants and the surfactants must be kept low.
- The micro-emulsion systems are not that much suitable for the intravenous use due to the toxicity of the formulation and till now only a very few studies have been reported on them.
- To reduce the toxicity of the micro-emulsion systems, the surfactants which are to be used are to be of "Generally-Regarded-as-Safe" (GRAS) class.

PROCESS OF PREPARATION

Micro-emulsions area unit ready once interfacial surface tension at the water/oil is reserved on identical squat level. Surface layer is set as identical considerable stretch in addition fluid absorption of surface-active-agent must remain high adequate to stretch surface-active-agent particles to be alleviated the micro-emulsion at an enormously very low interfacial surface tension.^{18,19}

Two chief technique are stated for the preparation of micro-emulsion, these are

1. Phase volumetric analysis technique

Micro-emulsions square measure ready by spontaneous emulsification technique, that is proved with facilitate of part diagrams. Part diagram creation is sensible approach to check complicated sequence of interaction that happens once totally different parts squares measure mixed. The facet of the part diagram is part equilibrium and separation of part boundaries. Utmost every so often pseudo-ternary part diagram are created to work out micro-emulsion region as quaternary part diagram is time overwhelming and tough to understand.^{20,21}

2. Phase-inversion technique

Phase-inversion of micro-emulsion occurs upon accumulation of spare of discrete phase. Phase-inversion results in radical physical amendments as alteration in element size that varies drug release. Throughout freezing, this method marks the purpose of nil impulsive curving and stripped physical phenomenon, instigation the development of excellently distributed oil droplets. Micro-emulsions is ready by measured adding of subordinate alkanols (pentanol, hexanol and butanol) to opaque emulsions to supply clear results including distributions of moreover mixture dispersions or w/o oro/w. They subordinate alkanols are unit referred to as co-surfactants. They subordinate the interfacial-surface-tension among Water and Oil appropriately squat formerly impulsive development.^{20,22,23}

CHARACTERIZATION OF MICRO-EMULSION

There are various techniques by which micro-emulsions are characterized. Because the micro-emulsions are very complex, they have various components involved in their systems, they have a very large variety of structures and also there are various limitations attached to their methods of characterization, it is very difficult to characterize micro-emulsions, but their characterization data is very much important used for their viable manipulation. Hence, corresponding revisions by means of the grouping of numerous methods remain essential to acquire an impressive sight of the structure and the Physico-chemical assets of the micro-emulsions.^{24,25}

For physico-chemical characterization of micro-emulsion the basic components are:

- The dimension and the microstructure of the micro-emulsion.
- Phase behavior and phase stability.
- The local molecular rearrangement.
- The surface features like charge distribution and the specific area.
- Shape.
- Interface and changing aspects.

From these assets, Interface and changing aspects and the particle size are very much important as many general properties of the micro-emulsions are governed by them. There are various parameters on which the drug release from the micro-emulsions depends such as droplet size, Oil liquid section magnitude relation.

COMPONENTS OF MICRO EMULSION

Several components are used in the preparation and expansion of micro-emulsions. Mostly Surface-Active Agent and Oil are used in Micro-emulsion. Chief components of micro-emulsion are²⁶⁻²⁸

Aqueous stage

Commonly, the aqueous stage comprises preservatives and hydrophilic active components. Occasionally Buffer solutions are used as aqueous stage.

Oil stage

Oil is the greatest important components of micro-emulsion for the reason that it can solubilize the mandatory dose of the Lipophilic Drug. Oil is well-defined as any liquid consuming squat polarity and squat miscibility with water. It also increases the fraction of lipophilic drug elated via the Intestinal-Lymphatic-System.²⁹

Surfactant (surface-active-agent)

Surfactant means a substance which shows some Interfacial or Superficial activity and used to reduce the Interface or Surface tension. It has empathy for Polar & Non-Polar Solvents. Surface-active- agent are the particles that comprise a Polar head group and a Polar tail.

Several types of surfactants that assistance in the liberal progress of micro-emulsion system are.³⁰⁻³¹

1. Cationic-Surfactant
2. Anionic-Surfactant
3. Non-Ionic-Surfactant
4. Zwitterionic-surfactants.

EVALUATION OF THE MICRO-EMULSIONS

Visual Inspection

By the visual inspection we can check the properties such as fluidity, homo-genicity and optical clarity.

Percent Transmittance Test (Limpidity Test)

The Percent Transmittance Test of the micro emulsion can be measured spectrophotometrically using spectrophotometer.³²

Measurements of Droplet Size

Size examination of micro-emulsion can be obtained by Dynamic-Light-Scattering experiments or electron microscopy. The polydispersity can be done by the similar Instrument.^{33,34}

Zeta-Potential Dimensions and Globule-Size

Zeta-Potential and Globule-Size of the micro-emulsion can be resolute by Dynamic-Light-Scattering, via a ZETASIZERHAS-3000.³⁵

Examination Under cross-polarizing Microscope

The nonappearance of fringence on the way to eliminate Liquid-Crystalline-Systems, the micro-emulsion must be examined under cross polarizing microscope.³⁶⁻³⁷

Constancy studies (Stability studies)

Physical stability of the micro-emulsion should be resolute beneath totally different storing surroundings (four, twenty five and forty °C) throughout twelve months. Recent preparations similarly by means of those that have been reserved beneath several strain situations intended for prolonged period of time were imperiled to Droplet Dimensions Delivery Examination. Conclusion of surface-active-agent& their attention on size of drop is also to be calculated.³⁸

pH of the Micro-emulsion

Different samples of the micro-emulsions are taken in the sample tubes. Then a micro pH-meter is employed to check the Ph-scale of the various samples. Since the pH-scale of the preparation is that the issue upon that the micro-emulsion Bioavailability and the constancy of the drug over micro-emulsion by the permeation spot depends upon.³⁹⁻⁴¹

Scattering Methods

The Scattering methods is like little angle of neutron scattering, little angle of X-Ray-Scattering and Light-Scattering have create submissions in revisions of micro-emulsion assembly, significantly just in case of diluted mono-disperse spheres, once poly-disperse or focused systems like as those often seen in micro-emulsions.⁴²

TRANSMITTANCE EXAMINATION

Constancy of the adjusted micro-emulsion preparation with relevancy dilution was check by measuring transmission at a particular wavelength with a Ultra Violet Spectrophotometer.⁴³

IN-VITRO DRUG RELEASE

The diffusion study is often disbursed on a changed Franz-Diffusion cell, among capacity of 20mL. The Receptor section was occupied with of Buffer. The donor section was secure with plastic wrap membrane, holding the micro-emulsion preparation and also the basic drug solution, distinctly. At prearranged time intermission trials were reserved from the receptor section and examined for drug content, employing a Ultra Violet spectrophotometer at definite wavelength.^{44,45}

RESEARCH-WORK ON MICRO-EMULSIONS

Throughout the previous decade a lot of analysis work has remained carried out on micro-emulsions for many paths of drug administration. Research-work on micro-emulsions is concise in Table 1-3.

RESEARCH-WORK ON MICRO-EMULSIONS

Table 1: Research-Work on Oral route

Drug title	Path	Purpose/Result	Ref.no.
Piroxicam	Oral	Increased the solubility	46
Acyclovir	Oral	Improved bioavailability	47
Clopidogrel	Oral	Solubility enhancement	48
Glipizide	Oral	Enhance drug dissolution and drug bioavailability.	49
Hydroxysafflor yellow A	Oral	Improved oral bioavailability.	50

Table 2: Research work on transdermal route

Drug title	Path	Purpose/Result	Ref. no.
Diclofenac	Transdermal	Permeability enhancement	51
Prilocaine HCL	Transdermal	Improved the solubility	52
Estra-diol	Transdermal	Enhancement in solubilization	53
Ketoprofen	Transdermal	Improved the solubility	54
Terbinafine	Transdermal	Permeability enhancement	55
Clonixic acid	Transdermal	For better absorption	56
Apomorphine-HCL	Transdermal	Improved the permeability	57
Ligustrazine phosphate	Transdermal	Increased permeation rate.	58

Table 3: Research-Work on other routes

Drug title	Path	Purpose/Result	Ref.no.
Chloramphenicol	Ocular	Enhancement of permeability	59
Fenofibrate	Self-Micro-emulsifying	Enhanced the solubility	60
Dexamethasone	Topical-Ocular	Improved the Bioavailability	61
Carbamazepine	Intra-nasal	Improved bioavailability	62
Aceclofenac	Dermatological	Improved the solubility	63
Timolol	Ophthalmic	For better absorption	64
Ibuprofen	Topical	Enhanced the solubility	65
Progesterone	Dermal	Increased the chemical-Stability	66

CONCLUSION

Micro-emulsions stand having a huge and substantial potential in Drug Delivery in addition as within the manufacturing process. The character of micro-emulsion in as long as innovative solutions to beat the issues of deprived aqueous solubility of highly oleophilic drug complexes and deliver high, more reliable and reproducible bioavailability. Current analysis work is concentrated on the making of safe, economical and extra companionable micro-emulsion elements which are able to any improve the value of those innovative vehicles. Micro-emulsions are used to attain Drug Targeting until now trials remain, mostly as of the films of barriers that these systems essential to overcome to range to the target. Nowadays micro-emulsions are shown to be ready to defend liable drug, controlled drug release, increase drug solubility, increase bioavailability, reduce patient variability, increase the rate of absorption, helps to solubilize the lipophilic drugs and several routes and also can be used to distribute the goods, useful in taste hiding, provides & increases the patient compliance. So, usage of micro-emulsion Based-Delivery-Systems is the most attractive and suitable zone of analysis, contribution not only many trials to beat but potential unexpected assistances.

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