

MICROEMULSION: A NOVEL APPROACH FOR IMPROVED DRUG DELIVERY

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ABSTRACT

Microemulsion are liquid dosage form which is biphasic in nature; they include the combination of oil and water as one formulation with the help of surfactants (Polyoxyethylene/Polysorbate/Tween 20,40,60,80) and co-surfactants (Ethanol, propanol, Isopropanol, butanol), which act as surface acting agent whereby reducing the surface tension between the two component (water and oil). Such agents form a clear, isotropic and thermodynamically stable with the same physical properties in all directions. As the name suggests microemulsion is emulsions having a less particle size compared to the normal emulsion formulations, the particle size ranges from (10-100nm) which are far more less than an emulsion particle size of (1-10mm). A microemulsion is potential drug

carrier for the various route of administration which includes: topical, nasal ophthalmic, drug targeting, cellular, brain, and other different drug delivery systems, where it has an advantage compared to other dosage forms by its ability to improve bioavailability, promotes taste masking and also absorption rate. In order to fully understand the full concept of the microemulsion, this article explains briefly the major key regarding microemulsion and the main basic idea behind it with reference to the scientific facts.

KEYWORDS: microemulsion, biphasic, isotropic, clear, particle size.

INTRODUCTION

Microemulsions are thermodynamic, clear mixture of two immiscible liquids like oil and water having uniform physical properties in all directions, which are stabilized by lowering

the surface tension between the two liquids using surfactants and sometimes co-surfactant to help enhance the effectiveness of the surfactant.^[1]

A microemulsion contain dispersed and continuous phases, the dispersed phase typically comprises of small individual droplets having a diameter of fewer than 100 nanometres and very low oil/water interfacial tension because the droplet is less than 25% of the wavelength of the visible light. Emulsions and microemulsions both include stabilizing of two immiscible liquid in their preparation by the help of surfactant. Their main difference lies in the size and shape of the particle in dispersed phase, in microemulsion the particle size is between (10-100nm) while emulsion droplet size is (1-20micrometer).^[1,2]

Another vital difference is appearance; emulsions are cloudy while microemulsions are clear and transparent. In addition, their preparation process emulsions require a large amount of energy while microemulsions do not. Microemulsions include the dispersion of nanometre-sized materials droplets of the two immiscible liquids within the liquids which is promoted by surfactants and co-surfactants.^[2]

For many years many studies have been promoted on the formation and the stability activity of these immiscible liquids oil in water dispersion (o/w) or water in oil (w/o) dispersion system. However, cosmetic industries and the formulators pursue and develop the most effective and simple cosmetically standard and functional product which finally formulated as o/w or w/o dispersion called microemulsions.^[2,3] These adaptable systems currently capture the interest of great technology and science to the researchers because of their ability to incorporate a wide range of drugs molecules both hydrophobic and hydrophilic due to the presence of both lipophilic and hydrophilic province. These versatile delivery systems provide the protection against the instability problems which include oxidation, enzymatic hydrolysis and promote the solubilizations activity of the lipophilic drugs and hence increase the bioavailability.^[3]

In addition to the oral and intravenous delivery, microemulsion can be formulated in other different routes like ophthalmic, dental, virginal and topical and such formulations are experiencing very active development as shown by numerous publications.

HISTORY

The concept of microemulsion come into existence by Schulman and hoar in the early 1940s, they prepared the first microemulsion by dispersing oil in an aqueous surfactant solution whereby adding alcohol as a cosolvent, resulting in a transparent and stable formulation.^[1, 9]

The theory behind the formulation was later confirmed with the use of various techniques which result in the promotion of the definition given by Attwood; which says “a microemulsion is a system containing water, oil and a substances with possesses both lipophilic and hydrophilic properties (surfactant and co-surfactant) which is a transparent, single optically isotropic and thermodynamically stable liquids”.^[1]

Table 1^[2]: Comparison of Microemulsion With Emulsion.

| S.No | Property | Microemulsion | Emulsion |
|------|---------------------|--|--|
| 1 | Appearance | Transparent/translucent | Cloudy |
| 2 | Optical isotropy | Isotropic | Anisotropic |
| 3 | Interfacial tension | Ultra low | High |
| 4 | Microstructure | Dynamic (interface is continuously and spontaneously fluctuating | Static |
| 5 | Droplets size | 20-200nm | >500nm |
| 6 | Stability | Thermodynamically stable | Long shelf-life thermodynamically unstable (kinetically will eventually phase separation |
| 7 | Phases | Monophasic | Biphasic |
| 8 | Preparation | Facile preparations ,relatively lower cost for commercial production | Require a large input of energy |
| 9 | Viscosity | Low viscosity with Newtonian behaviour | Higher viscosity |

Classification of Microemulsion

There are three types of a microemulsion which are formed based on their composition

- a. Oil in water microemulsions: wherein oil droplets are dispersed in the continuous aqueous phase.
- b. Water in oil microemulsions wherein water droplets are dispersed in the continuous oil phase.
- c. Bicontinuous microemulsions wherein microdomains of oil and water are interdispersed within the system.^[3]

In all the three types of microemulsions, surfactant or cosurfactant are used in stabilizing the interfacial tension between the two phases (oil and aqueous).^[4]

Winsor classification of microemulsions

Winsor classified microemulsions based on the situation occurs by mixing oil, water, and amphiphiles as shown below:

Type – I System

It comprises of O/W microemulsions at equilibrium with the excess oil phase. The surfactant is likely soluble in water and oil-in-water (O/W) microemulsions form (Winsor I). The surfactant rich water phase coexists with the oil phase where the surfactant is only present as monomers at small concentrations.^[4]

Type – II

It involves W/O microemulsions in equilibrium with the excess water phase. The surfactant is mainly in the oil phase and water-in-oil (W/O) microemulsions form the surfactant with oil-rich phase coexists with the surfactant of poor aqueous phase (Winsor II).

Type – III

It consists of the microemulsion in equilibrium with both excess water and oil phases.

Winsor III or middle phase microemulsion is a three-phase system where the surfactants of rich middle phases coexist with both excess water and oil surfactant poor phase.

Type – IV

A single-phase (isotropic) micellar solution, that forms upon addition of a sufficient quantity of amphiphile (surfactant plus alcohol).^[3]

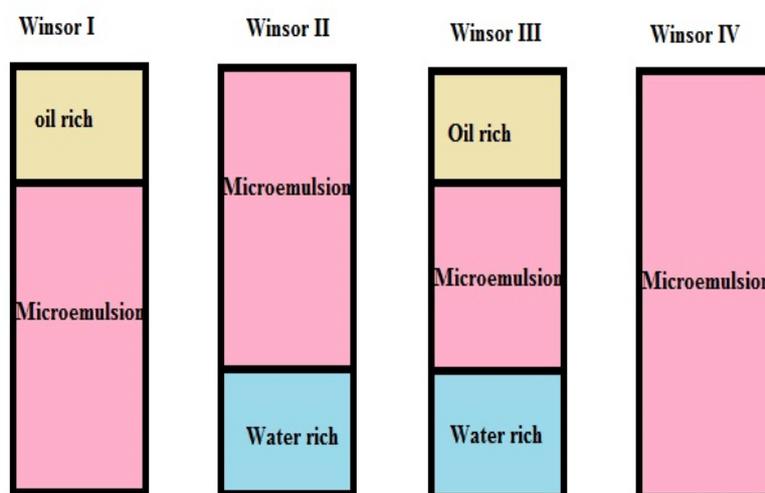


FIG.1.

Advantages of Microemulsion Based System

The microemulsion is a potential drug carrier for the various route of administration, where it has an advantage compared to other dosage forms.^[5]

- Enhance the absorption rate
- Decrease variability in absorption
- increase solubilization of the lipophilic drug
- Increases bioavailability
- Various routes of administration like tropical, oral and intravenous can be used to deliver the product Rapid and efficient penetration of the drug moiety^[6]
- enhance taste masking
- it protects the drugs from hydrolysis and oxidation process as a microemulsion in the oil phase (o/w) is not affected by water and air
- Liquid dosage form increases patient compliance.^[5]
- Less amount of energy requirement

Disadvantages of Microemulsion Based Systems

- High melting substances used in the system are having a limited solubilizing capacity.^[5]
- The surfactant should be nontoxic for use in pharmaceutical applications.
- Environmental factors like temperature and pH affect the stability nature of microemulsion.^[4]

Limitations

The following are factors which limit the use of microemulsion on pharmaceutical purposes:

- The concentration of surfactants and co-surfactants used must be kept low for toxicological reasons.^[5, 6]
- Phase separation instability
- For intravenous use, the demand for toxicity on the formulation is rigorous and very few studies have been reported so far.
- Use of those surfactants which are included in “generally regarded as safe” (GRAS) category can reduce toxicity.^[4]

Components of Microemulsion System

Microemulsion formulation as said in the introduction involves the coexisting of a different component (oil, water, and other excipients) which are stabilized using surfactant or co-surfactants, such components should be biocompatible, nontoxic and clinically approved.^[5]

The component is selected based on its presence in ‘generally regarded as safe’ (GRAS) category^[6]

The following are the major component used in the microemulsion formulation:

- I. Oil phase
- II. Aqueous phase
- III. Primary surfactant
- IV. Secondary surfactant (co-surfactant)
- V. Co-Solvent

I. Oil phase

The oil component is one of the major excipients in the microemulsion formulation not only because it solubilizes the required amount of dose in lipophilic drug, but it also improves the amount of lipophilic drug transported through the intestinal lymphatic system, thereby increasing the absorption rate from GI track depending on the molecular properties of triglyceride.^[7]

The oil region affects the curvature by its ability to penetrate and swell the tail group region of the monolayer surfactant. Short chain oils penetrate the tail group region to a larger extent than long alkane chain resulting in an increase in negative curvature and less effective HLB.^[6,7]

Following are the commonly used oil in the formulation of microemulsion

- Saturated fatty acid- example lauric acid, myristic acid, capric acid
- Unsaturated fatty acid- example oleic acid, linoleic acid, linolenic acid
- Fatty acid ester-ethyl or methyl esters of lauric, myristic and oleic acid.

Saturated and unsaturated fatty acids have the ability to enhanced penetration on their own Fatty acid esters have also been employed as the oil phase. Lipophilic drugs are preferably Solubilise in o/w microemulsions. Oil is selected according to the solubility of the drug, resulting in a decrease in volume of the formulation to deliver the therapeutic dose of the drug in an encapsulation form.^[7]

II. Aqueous phase

The aqueous phase may contain hydrophilic active ingredients and preservatives. Buffer solutions are used as an aqueous phase by some researchers.

Water is most commonly used as an aqueous phase. The pH of the aqueous phase always needs to be adjusted due to its considerable impact on the phase behaviour of microemulsions.

For microemulsion formulation for parenteral administration, the aqueous phase should be isotonic to blood which is usually adjusted by sodium chloride, glycerol, dextrose, and sorbitol.

III. Surfactants

The surfactant is also called surface active agents, these compounds lower the surface tension (interfacial tension) between the water and oil in the formulation. As surfactants adsorb they break this barrier between the two liquids and improve their stability.

Surfactants used to stabilize the microemulsion system may be;

- I. Non-ionic
- II. Zwitterion
- III. Cationic
- IV. Anionic surfactants.

Combinations of these, particularly ionic and non-ionic, can be very effective at increasing the extent of the microemulsion region.^[8]

- a) Non-Ionics include polyoxyethylene surfactants such as Brij 35 (C12E35) or sugar esters such as sorbitan monooleate (Span 80). Phospholipids are notable.
- b) Zwitterionic surfactants exhibit excellent biocompatibility. example Lecithin preparations they are derived from a variety of sources including soybean and egg are available commercially and contain diacyl phosphatidylcholine as its major constituent.
- c) Cationic surfactants: Quaternary ammonium alkyl salts form with hexadecyltrimethylammonium bromide (CTAB), and the twin-tailed surfactant didodecylammonium bromide (DDAB) are amongst the most well-known.
- d) Anionic surfactant: The most widely studied is probably sodium bis-2-ethylhexylsulphosuccinate (AOT) which is twin-tailed and is a particularly effective stabilizer of w/o microemulsions.^[5,8]

In the formation of microemulsion the surfactant may be ionic or non-ionic, which determines the stabilizing interactions of the hydrophilic end of the surfactant with the

aqueous phase. Thus, while a non-ionic surfactant is stabilized by dipole and hydrogen bond interactions with the hydration layer of water on its hydrophilic surface, the anionic surfactant is additionally stabilized by the electrical double layer. Thus, the effect of salt concentration on the stability of an emulsion or a microemulsion is more profound in the case of ionic surfactant than non-ionic surfactants.^[3,8]

Non-ionic surfactants are generally considered for oral formulations, The commercially available solubilized oral formulations include polyoxyl 35 castor oil (Cremophor EL), polyoxyl 40 hydrogenated castor oil (Cremophor RH 40), polysorbate 20 (Tween 20), polysorbate 80 (Tween 80), d- α -tocopherol polyethylene glycol 1000 succinate (TPGS), Solutol HS15, sorbitan monooleate (Span 80), polyoxyl 40 stearate, and various polyglycolized glycerides including Labrafil M-1944CS, Labrafil M2125CS, Labrasol, Gellucire 44/14, etc.

In general, the screening of surfactant can be done with the help of HLB (hydrophilic-lipophilic balance) values. The HLB contains a given value which suggests the types of microemulsion to form whether o/w or w/o type.

Table 2: HLB ranges and the typical applications of related surfactants.^[3]

| HLB values | Applications |
|------------|------------------------------|
| 1-3.5 | Antifoams |
| 3.5-8 | Water in oil emulsion |
| 7-9 | Wetting and spreading agents |
| 8-16 | Oil in water emulsions |
| 13-16 | Detergents |
| 15-40 | Solubilizer |

IV. Co-surfactants

The role of co-surfactant is to allow the interfacial film region adequately flexible to attach to different curvature required to form microemulsion over a wide range of composition. In single film surfactant, the lipophilic chain of the surfactant should be sufficiently short or contain fluidizing group like unsaturated bonds. Short to medium chain alcohol groups (C3C8) are commonly added as co-surfactants which reduce the interfacial tension between the phases and increase the fluidity of the interface. Typically co-surfactants are short chain alcohol compounds (ethanol to butanol), glycols like propylene glycol amine or acids.^[9]

The following are the main role of co-surfactant in microemulsion formulation:

- 1) Improve the fluidity of the interface.
- 2) Destroy the liquid crystalline or gel structure which affects the formation of the microemulsion.
- 3) Adjust HLB value

V. Co-solvents

The formulation of stable microemulsion mainly required a relatively high concentration of surfactant (more than 30% w/w). cosolvent are Organic solvents such as, ethanol, propylene glycol (PG), and polyethylene glycol (PEG) which are used in the dissolving large amount of either hydrophilic or lipophilic surfactants in microemulsion formulation, they sometimes act as co-surfactants^[4]

Table 3: Common Examples of Excipients Used To Formulate Microemulsions^[5]

| Components | Examples |
|----------------|---|
| Oils | Saturated fatty acid-lauric acid, myristic acid, capric acid Unsaturated fatty acid-oleic acid, linoleic acid, linolenic acid Fatty acid ester-ethyl or methyl esters of lauric, myristic and oleic acid. Example:(Glyceryl Mono-anddicaprate, isopropylmyristate, sunflower oil, soyabean oil, Labrafac ®CC), surfactant (Cremophor ®EL, Labrasol®) |
| Surfactants | Polyoxyethylene/Polysorbate/Tween 20,40,60,80,; Sorbitan Monolaurate (Span), Soybean lecithin, egg lecithin, lyso lecithin, Sodium dodecyl sulphate (SDS), Sodium bis (2-ethylhexyl) sulphosuccinate (Aerosol OT), Dioctyl sodium sulphosuccinate, Sodium dexoycholate, Labrasol (Polyethylene glycol-8-caprylic acid), TritonX-100 |
| Co-surfactants | Ethanol, propanol, Isopropanol, butanol, pentanol, hexanol, sorbitol, n-pentanoic acid, n-hexanoic acid, n-butylamine, sec, butylamine, 2-aminopentane, 1,2-butanediol, Propylene glycol. Some newly evolved cosurfactants are as follows : Cremophor RH40 (polyoxyl 40 hydrogenated castrol oil), Plurololeique (polyglyceryl-6-dioleate), Plurolisostearique (isostearic acid of polyglycerol), Distearoylphosphatidyl ethanolamine-N-poly (ethyleneglucol)2000 (DSPE-PEG), Poloxamer Polyoxyethylene-10-oelyl ether (Brij 96V) Polysorbate 80 (Tween80) Span 20 Sodium monohexyl phosphate Sodium monoethyl phosphate N,N-Dimethyl dodecylamine-N-oxide (DDNO) N,N-Dimethyl octylamine-N-oxide (DONO) Cinnamic alcohol Cinnamic aldehyde |

Theories of Microemulsion Formation

For decades microemulsion formation and stability are mainly explain using three different approaches. They are as follows;

- Interfacial or mixed film theories.
- Solubilization theories.

- Thermodynamic treatments.^[9]

In the formulation of the microemulsion, the free energy involved is considered to depend on the ability of the surfactant to lower the surface tension of the oil/water interface and change in entropy of the system such that,

$$G_f = \gamma \Delta A - T \Delta S$$

Where,

G_f = free energy of formation

ΔA = change in the interfacial area of the microemulsion

ΔS = change in entropy of the system

T = temperature

γ = surface tension of oil-water interphase.^[10]

After the microemulsion is formulated the change in ΔA (interfacial area) is very large due to the formation of a large number of the very small droplet. For a microemulsion to be formed a negative value is required, it is recognized that while the value of ΔA is positive at all the times, it is very small and is affected by the entropic component.^[8,9]

However favorable entropic contribution is expected, arising from the other dynamic processes such as surfactant diffusion in the interfacial layer and monomer micelle surfactant exchange. Thus negative free energy of formation is formed when there is a large reduction in the surface tension which is accompanied by significant favorable entropic change.^[6]

Factors To Be Considered During Preparation of Microemulsion

The following are the main factors to be considered during microemulsion formulations

- The Selection of surfactants is an important process as an ultra-low interfacial tension (< 10⁻³ mN/m) is to be attained at the oil/water interface which is a critical requirement to produce microemulsions.^[10]
- The concentration of surfactant must be high enough to provide the number of surfactant molecules needed to stabilize the microdroplets to be produced by an ultra-low interfacial tension.
- The interface must be flexible or fluid enough to promote the formation of microemulsions.^[4]

Method of Preparation of Microemulsion

In theory, the arrangement of the emulsifier molecules (possibly aided by cosurfactant) occurs spontaneously. However, in some cases, energy is provided to the system to speed up the rearrangement of the surfactant molecules, or to overcome a small kinetic energy barrier.^[11]

There are three principle methods that may be used in microemulsion formation.

A. Low energy emulsification method

Microemulsion preparation can be achieved in three different low energy emulsification methods:

- Dilution of anion surfactant mixture with water
- Dilution of a water-surfactant mixture with oil
- Mixing all the components together in the final composition.

As each of these methods involves the spontaneous formation of microemulsions, the order of ingredient addition may determine the formation of the microemulsion. Research in our laboratory has found that the order of ingredient addition played a significant role in the formation of microemulsions using ethoxylated mono- and di-glycerides as surfactant, soybean oil as the oil phase, and 50% sucrose in 5% ethanol as the aqueous phase.^[11]

On dilution of solutions having different aqueous: surfactant ratios with oil, a one-phase transparent solution was only formed when the ratio of aqueous: surfactant was 60:40.

On dilution of solutions having different oil: surfactant ratios with the aqueous phase, one-phase transparent solutions were located at several locations within the pseudo-ternary phase diagram.

However, only one of these areas coincided with the one-phase area identified in Figure a. The importance of the order of addition of ingredients seems to be quite important in some systems. For giardiniera.

Pseudoternary phase diagrams of soybean oil, ethoxylated mono and diglycerides and sucrose/ethanol aqueous systems at 20°C.^[12]

A—dilution of aqueous/surfactant solutions with oil.

B—dilution of oil/surfactant solution with an aqueous solution. Arrows show the direction of dilution. One phase area is indicated by the heavy black line.

That is a water/decade/POE surfactant system, microemulsions could only be formed on dilution of an oil-surfactant mixture with water.^[10,12]

B. Phase inversion temperature (PIT) method

The PIT method for microemulsion formation is particularly useful when using ethoxylated non-ionic surfactants. When an o/w emulsion containing ethoxylated non-ionic surfactant is heated, the emulsion inverts to a w/o emulsion at a critical temperature, the PIT. At the PIT, the droplet size and the interfacial tension reach a minimum, and upon cooling while stirring, a stable o/w microemulsion forms.

C. High-pressure homogenization

Homogenization may also be used to form microemulsions; however, the process of emulsification is generally inefficient (due to the dissipation of heat). In addition, the homogenization process may be extremely limited as the water/oil/surfactant mixture may be highly viscous prior to microemulsion formation.^[12]

Characterization of Microemulsion

I. Droplet Size

The droplet size of the dispersed phase of the microemulsion must be less than 100nm, and the droplet size distribution can be determined by either electron microscopy or light scattering technique. this technique has been suggested as the most effective method of predicting the stability of the microemulsion.^[11]

Dynamic Light-Scattering Measurements

The DLS measurements are performed at 90° in a dynamic light-scattering spectrophotometer using a neon laser of wavelength 632 nm. The data is processed by the built-in computer with the instrument. Polydispersity: Polydispersity is studied using Abbe refractometer.

Phase analysis: The type of microemulsion forming the phase system (o/w or w/o) is determined by measuring the electrical conductivity using a conduct meter.^[8]

II. Viscosity Measurement

The composition of several Microemulsion viscosities is measured at different shear rates using Brookfield type rotary viscometer at different temperatures. The sample room of the instrument must be maintained at $37 \pm 0.2^{\circ}\text{C}$ by a thermobath, and the samples for the measurement are to be immersed in it before testing.^[6]

III. Stability Studies

Physical stability of microemulsion is usually determined under different storage conditions (4,25 and 40°C) for a period of 12 months.

Freshly prepared microemulsion and those stored under various stress conditions for an extended period of time are subjected to analysis of droplet size distribution. However, the effect of surfactant and their concentration on droplet size are also studied review paper.

Identification Test For Type of Microemulsions

Dilution test

If the microemulsion is diluted with water and remains stable no crack or separation, such formulation is said to be oil in water microemulsion. While if after diluted, the emulsion crack or phase separation occurs, such microemulsion is said to be water in oil^[10]

Staining test

Water-soluble and oil-soluble dye can both be used in the staining test.

When some oil-soluble dye is added to the microemulsion, the background becomes colored, it implies that the microemulsion is a water-in-oil type. If the droplets become colored, the microemulsion is the oil-in-water type. The same phenomenon applies to Water soluble dye such as methylene blue or amaranth is added to the microemulsion. A drop of Microemulsions is observed under a microscope. If the background is found to be blue /red and the globule appears to be colourless such formulation is said to be oil in water microemulsion.^[12, 9]

Dilutability test

The Microemulsions formed is diluted in 1:10, and 1:100, ratios with double distilled water to check if the system shows any signs of separation.

Zeta potential measurement

The Determination of Zeta potential in the microemulsion is done using a zetasizer dilution test. The test is to determine the type of microemulsion formed after formulation, the zetasizer contains electrodes which measures the electric charge within the formulations.^[13]

When the electrodes are pass through the formulation and the charge is positive such formulation is oil in water while if there is negative or neutral charge its water in oil type.^[8]

Note oil in water shows a positive charge because water is a good conductor it allows a free movement of electric charge.

Zeta potential is essential to study flocculation since electrical charges on particles influence the rate of flocculation.^[10, 8]

Applications

Microemulsion is used as following:

- Microemulsions as fuels.
- Microemulsions as cutting oils and corrosion inhibitors
- Microemulsions as coatings and textile finishing.
- Microemulsions in detergency.
- Microemulsions in agrochemicals.
- Microemulsions in food.
- Microemulsions in environmental remediation and detoxification.
- Microporous media synthesis (microemulsion gel technique).
- Microemulsions in analytical applications.
- Microemulsions as liquid membranes.
- Novel crystalline colloidal arrays as chemical sensor materials^[4]

CONCLUSIONS

Microemulsion is a clear formulation containing a dispersed phase of less than 100nm of its individual particle, having such smaller particle size leads to its thermodynamically stable in nature which is able to protect labile drug, control drug release, increase drug solubility, increase bioavailability and reduce patient variability. For many years till date different studies and researches promote the use of microemulsion formulations as drug delivery system, However, cosmetic industries and the formulators pursue and develop the most effective and simple cosmetically standard and functional product which finally formulated

as o/w or w/o dispersion type microemulsions. These adaptable systems currently capture the interest of great technology and science to the researchers because of their ability to incorporate a wide range of drugs molecules both hydrophobic and hydrophilic due to the presence of both lipophilic and hydrophilic province. These versatile delivery systems provide the protection against the instability problems which include oxidation, enzymatic hydrolysis and promote the solubilizations activity of the lipophilic drugs and hence increase the bioavailability. In addition to the oral and intravenous delivery, microemulsion can be formulated in other different routes like ophthalmic, dental, vaginal and topical and such formulations are experiencing very active development as shown by numerous publications. Recently many research work shows how the microemulsions have been promisingly used to improve the drug delivery system for its advantages include their thermodynamic stability, optical clarity, and ease of penetration.

Finally, the microemulsion is a broad concept which requires a lot of research program, as of now many of its aspect is not yet fully uncovered and such can change the complete aspect of drug formulation and delivery system with its potential.

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REFERENCES

1. Amul Mishra, Ridhi Panola, A.C. rana; microemulsions: as drug delivery system, journal of scientific and innovative research, 2014; 3(4): 467-474.
2. S. Madhav and d. Gupta: a review on microemulsion based system, international journal of pharmaceutical science and research, 2011; 2(8): 1888-1899.

3. Jaspreet kaur saini¹, ujjwal nautiyal¹, senthil kumar m¹, devendra singh², firoz anwar³: microemulsions: a potential novel drug delivery system, international journal of pharmaceutical and medicinal research, 2014; 2(1): 15-20.
4. Faizi muzaffar, u. K. Singh, lalit chauhan: review on microemulsion as futuristic drug delivery, international journal and pharmaceutical science, 2013; 5(3).
5. Santosh nemichand kale¹, sharada laxman deore; review on emulsion micro emulsion and nano emulsion, a multifaceted review journal in the field of pharmacy, 2017; 8(1): 39-47.
6. Jha s.k, dey s, karki r; microemulsions- potential carrier for improved drug delivery, asian journal of biomedical and pharmaceutical sciences, 2011; 1(1): 5-9.
7. John flanagan and harjinder singh; microemulsions: a potential delivery system for bioactives in food, critical reviews in food science and nutrition, 2006; 46: 221–237.
8. Tapan kumar giri, nitin giri goswami, vijay kumar jha; prospective and challenges of micro-emulsion as a novel carrier for drug delivery, journal of pharmascitech, 2013; 2(2): 56-61.
9. Kai lun lee; applications and use of microemulsions, department of chemical engineering and chemical technology, imperial college london, November, 2010.
10. P. Kumar and k. L. Mittal (editors), handbook of microemulsion science and technology, marcel dekker, new york, 1999; 1–3: & 8.
11. Vinod singh, bushettii s.s, appala raju s, rizwan ahmad, mamta singh and anupam bisht; a review microemulsions as promising delivery systems, indian journal of pharmaceutical education and research association of pharmaceutical teachers of india, submitted: 8-11-2010 revised: 14-1-2011 accepted: 25-4-2011.
12. Berry, natasha, "development and stability of microemulsions as carriers for nutraceuticals" Theses and dissertations. Paper, 2011; 679.
13. John klier, christopher j. Tucker, thomas h. Kalantar, and d. P. (patrick) green; properties and applications of microemulsions, *adv. Mater*, 23, December, 2000; 12.