



MICROEMULSIONS AS CARRIER FOR NOVEL DRUG DELIVERY: A REVIEW

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ABSTRACT

Microemulsions are excellent candidates as potential drug delivery system because of their improved drug solubilization, long shelf life and ease of preparation and administration. These versatile systems are thermodynamically stable, colloidal dispersion of water and oil stabilized by surfactant and cosurfactant. It provides protection against oxidation, enzymatic hydrolysis and improves the solubilization of lipophilic drugs and hence enhances their bioavailability. In addition to oral and intravenous delivery, they are amenable for sustained and targeted delivery through ophthalmic, dental, pulmonary, vaginal and topical routes. In this present review article, we discuss about the various advantages of microemulsions in pharmaceuticals, along with its preparation, characterization and research work carried out on microemulsions.

Keywords: Surfactant, Lipophilic drugs, Microemulsions, Thermodynamically stable, Bioavailability.

INTRODUCTION

The design and development of new drug delivery system with the intention of enhancing the efficacy of existing of drug is an ongoing process in pharmaceutical research. Since there are many types of drug delivery systems that have been developed, one in particular the colloidal drug delivery system has great potential for achieving the goal in drug targeting. The concept of microemulsions or Micellar emulsion was first introduced by Hoar and schulman in 1943. They prepared the first microemulsions by dispersing oil in an aqueous surfactants solution and adding an alcohol as a cosurfactant, leading to transparent stable formulation¹. Microemulsions are defined as a system of water, oil, and amphiphile which is a single optically isotropic and thermodynamically stable liquid solution². Microemulsions forms spontaneously with an average droplet diameter³ of 10 to 140 nm. Microemulsions contain definite boundary between oil and water phases at which surfactant is located. Conventional surfactant molecules comprised polar head group region and an apolar tail region. Microemulsions may be asymmetric in shape, frequently adopting the shape of prolate ellipsoid.⁴ Microemulsions can be applied as liquid membrane carriers to transport lipophilic substance through a aqueous medium or to carry hydrophilic substances across lipoidal medium.⁵ As the size of the particle is much smaller than the wavelength of visible light, Microemulsions are transparent and structure cannot be observed through an optical microscope⁶. Microemulsions are liquid behave as a newtonian liquid .They are not very viscous⁷.

ADVANTAGES OF MICROEMULSIONS⁸⁻¹⁵

Microemulsions system has considerable potential to act as a drug delivery vehicle by incorporating a wide range of drug molecules.

- (1) Good thermodynamically stable and inexpensive.
- (2) It is used in the wide range of pharmaceuticals and cosmetics formulation.
- (3) It is used as a vehicle for topical, oral, nasal and transdermal applications.
- (4) It is used as bioavailability enhancers for poorly water soluble drug.
- (5) It acts as a penetration enhancers and 'supersolvents' of drug.
- (6) Long shelf life.
- (7) Wide applications in colloidal drug delivery systems for the purpose of drug targeting and controlled release
- (8) Helpful in taste masking.

DISADVANTAGES OF MICROEMULSIONS¹⁶⁻¹⁸

- (1) The main problem in a microemulsions application is a high concentration and a narrow range of physiologically acceptable surfactants and co-surfactants.
- (2) It has limit potential topical application due to their toxic and irritant properties of component.
- (3) Large surfactant concentration (10-40%) determines their stability.
- (4) It is poor palatability due to the lipid content leading to the poor patient compliance. Moreover due to their water content, Microemulsions cannot be encapsulated in soft gelatin or hard gelatin capsules.



STRUCTURE OF MICROEMULSIONS

Microemulsions or Micellar emulsion are dynamic system in which the interface is continuously and spontaneously fluctuating.¹⁹ Structurally, they are divided in to oil in water (o/w), water in oil (w/o) and bicontinuous microemulsions. In w/o microemulsions, water droplets are dispersed in the continuous oil phase while o/w microemulsions are formed when oil droplets are dispersed in the continuous aqueous phase. In system where the amounts of water and oil are similar, the bicontinuous microemulsions may result.²⁰ The mixture oil water and surfactants are able to form a wide variety of structure and phase depending upon the proportions of component.

TYPES OF MICROEMULSIONS

The Microemulsions are three types, they are

1. Oil in water (o/w) or Winsor I, 2. Water in oil (w/o) or Winsor II, 3. Bicontinuous microemulsions or Winsor III (Fig. 1) In o/w microemulsions the volume fraction of oil is low conversely in w/o emulsion the volume fraction water is low and the oil droplets in o/w microemulsions are surrounded by the electrical double layer, which can extend into the external phase for a considerable distance up to 100 nm, depending up on the electrolyte concentration.²¹ In bicontinuous Microemulsions the amounts of water and oil ratios are similar.²²



Figure 1: Types of Microemulsions.

THEORETICAL BASIS OF MICROEMULSIFICATIONS²³

When surfactants is added to a mixture containing equal amounts of oil and water either W/O or O/W emulsion will form depending on the molecular interaction of the surfactant with both the oil and water. Different interaction strengths on the both the sides of the surfactant film induce a tension gradient across the surfactant membrane and consequently produce curvature. A geometrical model has been proposed to describe quantitatively the correlation between the structure of surfactant aggregates and geometric packing of surfactants at the interface is called as packing ratio or critical packing parameter (CPP). CPP defines as the ratio of cross sectional area of hydrocarbon chain to that of the polar head of the surfactant molecule at the interface, i.e.

$$V/a_o l_c$$

Where

V= Volume of the hydrocarbon chain of surfactant

a_o = optimal cross sectional area per polar head in a planar interface

l_c = approximately 80- 90 % of the fully extended length of the surfactant chain.

A greater cross sectional area of the tail than that of the head ($V/a_o l_c > 1$) would favour the formation of w/o droplets where as smaller cross area of the tail than that of the head ($V/a_o l_c < 1$) would favour the formation of O/W droplets. A planar interface dictates $V/a_o l_c = 1$, leading to the formation of lamellar structure. Many approaches have been used to explore the mechanisms of microemulsions formation and stability. Some emphasise the formation of an interfacial film and the production of ultra low interfacial tension (Mixed film theories) other emphasise the monophasic nature of many micro emulsions (Solubilisation theories). Thermodynamic theories consider the free energy the formation of microemulsions and the bending elasticity of the film. No one approach alone covers all aspect of microemulsions structure and stability and all have a place in the overall understanding of microemulsions.

Factors to be considered during preparation of Microemulsions²⁴

There are three important conditions, such as

1. Surfactants must be carefully chosen so that an ultra low interfacial tension can be attained at the oil/water interface which is a prime requirement to produce microemulsions.
2. 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.
3. The interface must be flexible or fluid enough to promote the formation of Microemulsions.

DIFFERENCE BETWEEN EMULSION AND MICROEMULSIONS²⁵⁻²⁷

Emulsions and Microemulsions (Fig.2) are both stable dispersions of oil-in-water or water-in-oil. Surfactants are the principal agents that enable oil and water to mix. Emulsions are stable dispersions of immiscible liquids, but they are not thermodynamically stable. The following properties shows the different between emulsion and Microemulsions. (Table 1).



Figure 2: Emulsion and Microemulsions preparation.

Table 1: Difference between emulsion and Microemulsions

Property	Emulsion (Macro emulsion)	Microemulsions
Appearance	Cloudy	Transparent
Optical isotropy	Anisotropic	Isotropic
Interfacial tension	High	Ultra low
Microstructure	Static	Dynamic
Droplet size	>500 nm	20-200nm
Stability	Thermodynamically unstable	Thermodynamically stable and long shelf life
Phases	Biphasic	Monophasic
Preparation	Require a large input of energy	Facile preparation
Cost	Higher cost	Lower cost
Viscosity	High viscosity	Low viscosity with Newtonian behavior
Turbidity	Turbid	Transparent
Cosurfactant used	No	Yes
Surfactant concentration	1-20 %	>10%
Size range	0.5 – 5 μ	<0.1 μ
Molecular packing	Inefficient	Efficient
Micelle diameter	20 nm +	3- 20 nm
Contact position	Direct oil / water contact at the interface	No direct oil in water contact at the interface

Table 2: Microemulsions based marketed product

Brand name	Composition	Manufactured by
Sandimmune Neoral [®]	Cyclosporin A	Novartis
Fortovase [®]	Saquinavir	Roche laboratories
Norvir [®]	Ritonavir	Abbott Laboratories

Table 2: Research work carried out on microemulsions

S.No	Category	Drug	Route	Benefit
1.	Analgesics	Flurbiprofen	Parenteral	Increased the solubility
2.	Antiparkinson Agents	Apomorphine Hcl	Transdermal	Increased the permeability
3.	Analgesics	Ketoprofen	Transdermal	Enhancement of permeability
4.	Antifungal	Flucanazole	Topical	Reduce GIT adverse effect
5.	Anti hyperlipidemic	Fenofibrate	Self micro emulsifying	Increasing the solubility
6.	Anticholesteremic Agents	Estradiol	Transdermal	Improvement in solubilization
7.	Antihypertensive Agents	Timolol	Ophthalmic	For better absorption
8.	Analgesic	Ibuprofen	Parenteral	Increased the solubility
9.	Cyclooxygenase Inhibitors	Piroxicam	Oral	Increase the solubility
10.	Hormones	Progesterone	Dermal	Increase the chemical stability
11.	Analgesic	Ibuprofen	Topical	Increasing the solubility
12.	Antifungal Agents	Terbinafine	Transdermal	Permeability enhancement
13.	Antifungal Agents	Amphotericin	Parenteral	For better absorption
14.	Glucocorticoids	Dexamethasone	Topical ocular	Enhanced the bioavailability
15.	Antifungal Agents	Itraconazole	Parenteral	For better absorption
16.	Local Anesthetics	Prilocaine Hcl	Transdermal	Increased the solubility
17.	NSAID	Diclofenac	Transdermal	Permeability enhancement
18.	Anti-Bacterial Agents	Chloramphenicol	Ocular	Increase the solubility
19.	Serotonin Agonists	Sumatriptan	Intranasal	Enhance the bioavailability

COMPONENTS OF MICROEMULSIONS²⁸

Microemulsions are isotropic system, which are difficult to formulate than ordinary emulsion because their formulation is highly specific process involving spontaneous interaction among the constituent molecules. Generally, the Microemulsions formulation involves the following components,

a. Oil phase

Toluene, cyclo hexane, mineral or vegetable oil, silicone oil, or esters of fatty acids etc. widely used as oil component.

b. Aqueous phase

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



c. Surfactant

In order to reduce the interfacial tension, surfactant is necessary one. Hence surfactant with a balanced hydrophilic and lipophilic property (HLB) is desirable. The selection of surfactant must be

1. Reduce the interfacial tension during the preparation of Microemulsions.
2. Provide a flexible film that can readily deform round small droplets.
3. Appropriate hydrophile-lipophile character to provide the correct curvature at the interfacial region for the desired Microemulsions type o/w, w/o or bicontinuous.

1. Primary surfactant

The surfactant are generally ionic, non ionic or amphoteric. The surfactants chosen are generally from the non ionic group because of their good cutaneous tolerance. Only for specific case amphoters are being investigated.

2. Secondary surfactant

It is otherwise called as cosurfactant. The cosurfactant originally used were short chain fatty alcohol such as pentane, hexanol, benzyl alcohol. These are most often polyols, esters of polyols derivatives of glycerol and organic acids, Poloxamer, Polysorbate 80, Span 20 Cinnamic alcohol, Cinnamaldehyde.²⁹ Their main purpose is to make the interfacial film fluid by wedging themselves between the surfactant molecules.³⁰

Solubility studies of drug³¹

The solubility of drug in various oils (Glyceryl Mono-& dicaprate, isopropyl myristate, sunflower oil, soya bean oil, Labrafac® CC), surfactant (Cremophor® EL, Labrasol®), and co-surfactants (Transcutol® P, isopropyl alcohol, PEG-600, and glycerol) was determined. Excess drug (100 mg) was added to each cap vial containing five millilitres each of the selected vehicle. After sealing the cap vials, the mixtures were shaken on a shaker at 25°C for 48 hours. Each vial was then centrifuged at 10 000 rpm for 10 minutes. The undissolved drug in the pellet, as well as the solubilised drug in the supernatant, was quantified by UV spectroscopy and the mass balance was obtained.

Construction of pseudoternary phase diagram

Pseudoternary phase diagrams of oil, surfactant or co surfactant and water were developed using the water titration method³². The mixtures of oil and surfactant or cosurfactant at certain weight ratios were diluted with water in a drop wise manner. For each phase diagram at a specific ratio of surfactant or cosurfactant a transparent and homogenous mixture of oil and surfactant and cosurfactant was formed by vortexing for 5 minutes. Then each mixture was titrated with water and visually observed for phase clarity and flowability. The concentration of water at which turbidity-to-transparency and transparency to turbidity transitions occurred was

derived from the weight measurements. These values were then used to determine the boundaries of the Microemulsions domain corresponding to the chosen value of oils, as well as the surfactant or cosurfactant mixing ratio. To determine the effect of drug addition on the microemulsions boundary, phase diagrams were also constructed in the presence of drug using drug-enriched oil as the hydrophobic component. Phase diagrams were then constructed using Tri plot v1-4 software.

PREPARATION OF MICROEMULSIONS

1. Phase titration method³³

Microemulsions are prepared by the spontaneous emulsification method (phase titration method) and can be depicted with the help of phase diagrams. Construction of phase diagram is a useful approach to study the complex series of interactions that can occur when different components are mixed. Microemulsions are formed along with various association structures (including emulsion, micelles, lamellar, hexagonal, cubic, and various gels and oily dispersion) depending on the chemical composition and concentration of each component. The understanding of their phase equilibria and demarcation of the phase boundaries are essential aspects of the study. As quaternary phase diagram (four component system) is time consuming and difficult to interpret, pseudoternary phase diagram is often constructed to find the different zones including Microemulsions zone, in which each corner of the diagram represents 100% of the particular component (Fig. 3). The region can be separated into w/o or o/w microemulsions by simply considering the composition that is whether it is oil rich or water rich. Observations should be made carefully so that the metastable systems are not included.

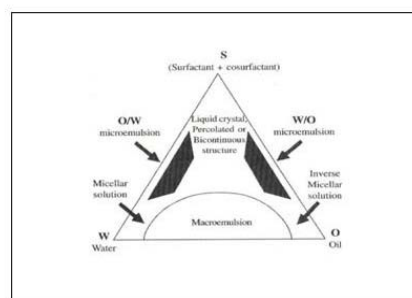


Figure 3: Pseudoternary phase diagram of oil, water, surfactant showing microemulsion region.

2. Phase inversion temperature method (PIT)

Phase inversion of microemulsions occurs up on addition of excess of the dispersed phase or in response to temperature²⁵. During phase inversion drastic physical changes occur including changes in particle size that can affect drug release both *in vivo* and *in vitro*. These methods make use of changing the spontaneous curvature of the surfactant. For the non ionic surfactant, this can be achieved by changing the temperature of the system, forcing a transition from an o/w microemulsions

at low temperature to a w/o microemulsions at higher temperature is called as transitional phase inversion. During cooling the system crosses a point of zero spontaneous curvature and minimal surface tension, promoting the formation finely dispersed oil droplets.

CHARACTERIZATION OF MICROEMULSIONS²⁵

The basic component in a physicochemical characterization of microemulsions systems are

1. Phase stability and phase behavior.
2. Microstructure, dimension.
3. Shape and surface features such as specific area, charge and distribution.
4. Local molecular rearrangement.
5. Interaction and dynamics.

Among these properties particle size, interactions, and dynamics are fundamental importance because they control many of general properties of microemulsions. The release of drug from Microemulsions depends on various process parameters like oil aqueous phase ratio, droplet size, the distribution of drug in the phases of Microemulsions system and rate of diffusion or absorption in both phases.²⁸

MARKETED MICROEMULSIONS^{34,35}

There are certain microemulsions which are commercially available in the market. (Table 2).

RESEARCH WORK CARRIED OUT ON MICROEMULSIONS³⁶⁻⁵⁴

In the last two decades research scientists have been tried for the preparation of microemulsions by using different types of active pharmaceutical ingredient with different routes of drug delivery. (Table 3)

EVALUATION OF MICROEMULSIONS

The microemulsions are evaluated by the following techniques, they are

(A) Measurement of pH

The pH values of Microemulsions were determined using digital pH meter standardized using pH 4 and 7 buffers before use.

(B) Globule Size Analysis of the Microemulsions

The average globule size of the microemulsions were determined by the photon correlation spectroscopy. Measurements were carried at an angle of 90° at 25°C. Microemulsions were diluted with double distilled water to ensure that the light scattering intensity was within the instrument's sensitivity range. Double distilled water was filtered through 0.45µm membrane filters prior to globule size determination.

(C) Measurement of electrical conductivity⁵⁵

The electrical conductivity of microemulsions was measured with a conductivity meter equipped with inbuilt

magnetic stirrer. This was done by using conductivity cell consisting of two platinum plates separated by desired distance and having liquid between the platinum plate acting as a conductor.

(D) Rheological studies

Changing the rheological characteristics help in determining the microemulsions region and its separation from other related structure like liquid crystals bicontinuous microemulsions are dynamic structure with continuous fluctuation occurring between the bicontinuous structure, swollen reverse micelle, and swollen micelle.

(E) Viscosity Measurements⁵⁶

Microemulsions are generally low viscosity systems. The viscosity measurements were performed using Brookfield viscometer at single mode (Spindle C-50). All the measurements were done in triplicate for 60 seconds at a temperature of 23.5°C.

(F) Polydispersity: This property is characterized by Abbe refractometer.

(G) Phase behavior studies

Visual observation, phase contrast microscopy and freeze fracture transmission, electron microscopy can be used differentiate microemulsions from liquid crystals and coarse emulsions. Clear isotropic one phase system are identified as microemulsions where as opaque system showing birefringence when viewed by cross polarized light microscopy may be taken as liquid crystalline system .

(H) Freeze thawing method⁴⁰

Freeze thawing was employed to evaluate the stability of formulations. The formulations were subjected to 3 to 4 freeze-thaw cycles, which included freezing at – 4°C for 24 hours followed by thawing at 40°C for 24 hours. Centrifugation was performed at 3000 rpm for 5 minutes. The formulations were then observed for phase separation. Only formulations that were stable to phase separation were selected for further studies.

(I) Scattering techniques

Scattering technique such as Small angle neutron scattering (SANS), Small angle x-ray scattering (SAXS), Dynamic light scattering (DLS) are used for studying Microemulsions structure especially on the size, shape and dynamics of the components.

(J) Nuclear Magnetic Resonance Studies⁵¹

The Fourier transform pulsed-gradient spin-echo (FT-PGSE) technique uses the magnetic gradient on the samples and it allows simultaneous and rapid determination of the self-diffusion coefficients of many components.

(K) Study of microstructure of Microemulsions⁵⁷

Transmission Electron Microscopy (TEM) is the most important technique for the study of microstructures of



microemulsions because it directly produces images at high resolution and it can capture any co-existent structure and micro-structural transitions.

There are two variations of the TEM technique for fluid samples.

1. The cryo-TEM analyses in which samples are directly visualized after fast freeze and freeze fracture in the cold microscope.
2. The Freeze Fracture TEM technique in which a replica of the specimen is imaged under RT conditions.

(L) Identification test for type of microemulsions⁵⁸

1. Dilution test

If the continuous phase is added in microemulsions, it will not crack or separate into phases. If water is added in o/w type of microemulsions it will remain stable.

2. Staining test

Water soluble dye such as methylene blue or amaranth was added in water and microemulsion was prepared with oil and surfactant. A drop of Microemulsions was observed under microscope. Background was found to be blue / red and globule will appear colorless respectively.

(M) Clarity test

It observed visually, because microemulsions are clear and transparent.

(N) Dilutability test

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

(O) Zeta potential measurement⁵⁹

It must be negative or neutral, which indicate that droplets of micro emulsion having no charge that is system is stable. Zeta potential is determined by using Zetasizer. Zeta potential is essentially useful for assessing flocculation since electrical charges on particles influence the rate of flocculation.

APPLICATION OF MICROEMULSIONS

Microemulsions are promising delivery systems that allow sustained or controlled drug release for percutaneous, peroral, topical, transdermal, ocular and parenteral administration. Enhanced absorption of drugs, modulation of the kinetics of the drug release and decreased toxicity are several advantages in the delivery process.⁶⁰

1. Microemulsions in ocular drug delivery⁶¹

Eye drops are the most used dosage form by ocular route, in spite of low bioavailability and the pulsed release of the drug. However, due to their intrinsic properties and specific structures, the microemulsions are a promising dosage form for the natural defence of the eye. Indeed,

because they are prepared by inexpensive processes through autoemulsification or supply of energy, and can be easily sterilized, they are stable and have a high capacity of dissolving the drugs. The *in vivo* results and preliminary studies on healthy volunteers have shown a delayed effect and an increase in the bioavailability of the drug. The proposed mechanism is based on the adsorption of the nanodroplets representing the internal phase of the Microemulsions, which constitutes a reservoir of the drug on the cornea and should then limit their drainage.

2. Microemulsions in Cosmetic preparation⁶²

In many cosmetic applications such as skin care products, emulsions are widely used with water as the continuous phase. It is believed that microemulsions formulation will result in a faster uptake into the skin. Cost, safety (as many surfactants are irritating to the skin when used in high concentrations), appropriate selection of ingredients (i.e. surfactants, cosurfactants, oils) are key factors in the formulation of microemulsions.

3. Microemulsions in biotechnology field

Many biocatalytic and enzymatic reactions are conducted in aqua-organic or pure organic as well as in biphasic media (i.e. polar media solubilizing enzymes and nonpolar media solubilizing a polar substituents). Their use is seriously limited, as they can inactivate or denature the biocatalysts. Recently, interest on Microemulsions is being focused for various applications in biotechnology, viz, enzymatic reactions, immobilization of proteins and bioseparation.

The potential advantages of employing enzymes in media of low water content, i.e. w/o microemulsions are: (i) increased solubility of nonpolar reactants; (ii) possibility of shifting thermodynamic equilibria in favour of condensation; (iii) improvement of thermal stability of the enzymes, enabling reactions to be carried out at higher temperature. Catalysis by a large number of enzymes in microemulsions media has been studied for a variety of reactions, such as synthesis of esters, peptides and sugar acetals; transesterifications; various hydrolysis reactions; glycerolysis; oxidation and reduction and steroid transformation.⁶³

4. Microemulsions in topical drug delivery

In conventional topical drug delivery basically involve either assisting or manipulating the barrier function of the skin (topical antibiotics, antibacterials, emollients, sunscreen agents) or breaching the horny layer at the molecular scale so as to direct drugs to the viable epidermal and dermal tissues without using oral, systemic or other therapies. Microemulsions have the ability to deliver larger amounts of water and topically applied agents into the skin than water alone or other traditional vehicles such as lotions or creams because they act as a better reservoir for a poorly soluble drug through their capacity for enhanced solubilization.⁶⁴ The role of penetration enhancers played by the amphiphilic



components of the Microemulsions and the internal mobility of the drug within the vehicle also contribute to the overall performance of Microemulsions in dermal or transdermal drug delivery.⁶⁵

5. Microemulsions in intranasal drug delivery

Intranasal Microemulsions is one of the focused delivery options for noninvasive drug delivery to systemic circulation. The researchers studied the brain uptake of nimodipine by intranasal administration of nonionic surfactant based Microemulsions and found three fold higher of nimodipine and higher ratios of AUC in brain tissues and cerebrospinal fluid to that in plasma.⁶⁶ In other studies, the intranasal delivery of Microemulsions of sildenafil citrate showed shorter t_{max} and higher AUC compared to the oral tablets in rabbits and higher relative bioavailability of sildenafil citrate.⁶⁷

6. Microemulsions in oral delivery⁶⁸

Microemulsions formulations offer the several benefits over conventional oral formulation for oral administration including increased absorption, improved clinical potency, and decreased drug toxicity. Therefore, Microemulsions have been reported to be ideal delivery of drugs such as steroids, hormones, diuretic and antibiotics peptides and proteins. However, most are difficult to administer orally and oral bioavailability in conventional (i.e. non-Microemulsions based) formulation of less than 10%, they are usually not therapeutically active by oral administration. Because of their low oral bioavailability, most protein drugs are only available as parenteral formulations. However, peptide drugs have an extremely short biological half life when administered parenterally, so require multiple dosing.

7. Microemulsions in parenteral drug delivery

Parenteral administration especially via the intravenous route of drugs with limited solubility is a major problem in industry because of the extremely low amount of drug actually delivered to a targeted site. Microemulsions formulations have distinct advantages over macroemulsion systems when delivered parenterally because of the fine particle Microemulsions is cleared more slowly than the coarse particle emulsion and, therefore, have a longer residence time in the body. Both o/w and w/o microemulsions can be used for parenteral delivery.

CONCLUSION

Microemulsions are an attractive technology platform for the pharmaceutical formulator as they are thermodynamically stable, possess excellent solubilization properties, and their formulation is a relatively straightforward process. These properties as well as their ability to incorporate drugs of different lipophilicity. Recently, several research papers have been published for the improvement of drug delivery, but still there is a need to emphasis on its characterization part including invitro evaluation. Besides this, research papers

shows higher percentage of surfactant used for the formation of microemulsions, irrespective of different routes of administration, but there is a lack of toxicological evaluation of the prepared microemulsions, which can be a broad research area in future.

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