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Microemulsion: As Excellent Drug Delivery System

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ABSTRACT

Today though the oral drug delivery system is dominant still it is found to be need of ideal transdermal drug delivery system. "A micro emulsion is a system of water, oil and an amphiphile which is a single optically isotropic and thermodynamically stable liquid solution". Microemulsions offer several advantages as drug delivery systems as these are thermodynamically stable and stability allows for self emulsification of the system with microemulsion acting as supersolvent of the drugs which are poorly or insoluble in water. They are preferred more as compared to conventional emulsions due stability. The dispersed phase mainly acts as the solvent for the water insoluble drug. Microemulsions have been proved to increase the cutaneous absorption of both lipophilic and hydrophilic API's when compared to conventional vehicles.

KEYWORDS

Microemulsion, Amphiphile, Thermodynamic stability.

INTRODUCTION

The microemulsion was first introduced by Hoar and Schulman in 1943; they prepared the first microemulsions by dispersing oil in an aqueous surfactant solution and adding an alcohol as a co-surfactant, leading to a transparent, stable formulation. The existence of this theoretical structure was later confirmed by use of various technologies, and we can today adopt the definition given by Attwood[7]. A microemulsion is an optically clear pre-concentrate containing a mixture of oil, hydrophilic surfactant and hydrophilic solvent which dissolves poor water soluble drug. Upon contact with water, the formulations spontaneously disperse (or 'self emulsifies') to form a very clear emulsion of exceedingly small and uniform oil droplets containing the solubilised poorly soluble drug.

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Since microemulsion increases the loading, bioavailability and penetration through various biological membranes of drug.

Microemulsions differ from emulsion in concern with the kinetic stability. The use of various combinations of surfactant and co surfactant makes microemulsion more kinetically ant thermodynamically stable. These are clear and less viscous than emulsions. The presence of surfactant and cosurfactant in the system makes the interfacial tension very low. Therefore, the microemulsion is thermodynamically stable and forms spontaneously, with an average droplet diameter of 1 to100 µm.7-9. Microemulsion requires less energy of preparation than emulsion.

The use optimum concentration of surfactant and cosurfactant reduces the surface tension and interfacial tension between droplets of oil. However microemulsion is very complex system with a microstructure which may get disrupted by small change in the concentration of components. The optimization of these

characters can be done by using the pseudoternary diagram and studying phase behaviour of system. Pseudoternary phase diagrams were constructed to examine the formation of oil in water microemulsions and microemulsion existing zone using three components. Pseudoternary phase diagrams were constructed keeping concentration of one component constant and varying the remaining 2 components. Titration method is normally used to determine the formation of microemulsion, if turbidity appeared followed by a phase separation, the samples were considered to be biphasic. If clear and transparent mixtures were visualized after stirring, the samples were considered monophasic. The samples were marked as points in the phase diagram. The area covered by these points was considered to be the microemulsion existence region. To determine the effect of drug on the microemulsion existing zone, phase diagrams were also constructed in the presence of drug using drug enriched oil as the hydrophobic component.

This review focuses on recent developments in the field of microemulsion technology with respect to drug delivery. The article summarizes the recently introduced patents on microemulsion systems and explores their potential in the delivery of poorly soluble drug compounds in particular in addition to their novel applications. Together with classical applications in detergency and lubrication, the field remains sufficiently important to continue to attract a number of scientists. From the fundamental research point of view, a great deal of progress has been made in the last 20 years in understanding microemulsion properties which gives its importance and need to be studied.

Merits of Microemulsion-based systems[9]

Microemulsions exhibit several advantages over conventional dosage form,

- Microemulsions are thermodynamically stable systems exactly apposite to emulsions and stability allows for self-emulsification of the system whose properties are not dependent on the process followed.
- Microemulsions act as 'supersolvents' of drug. Both hydrophilic & lipophilic drugs can be delivered by microemulsion.
- As compared to emulsion or suspension, the mean diameter of microemulsion droplets is below 0.22 m and hence such systems can be sterilized by filtration.
- Because of thermodynamic stability, microemulsions are easy to prepare and hence no significant energy contribution is required for the preparation. Microemulsions have low viscosity as compared to other emulsions
- The use of microemulsions as delivery systems can improve the efficacy of drug as the total dose is reduced thereby minimizing the side-effects.
- The formation of microemulsions is reversible. These may become unstable at low temperature & as temperature is brought to stability range, microemulsions are reformed.

Theories

The formation of microemulsion can be illustrate by three theories,

- interfacial or mixed film theories
- Solubilisation theory
- Thermodynamic treatment.

The surfactant lowers the interfacial tension between droplets of oil which gives the amount of free energy of microemulsion formulation and change in the entropy can be given by equation[19]

$$\triangle Gf = \gamma \triangle A - T \triangle S$$

Where, $\triangle Gf$ is the free energy of formation, γ is the surface tension of the oil–water interface,

$\triangle A$ is the change in interfacial area on microemulsification, DS is the change in entropy of the system which is effectively the dispersion entropy, and T is the temperature. It should be noted that when a microemulsion is

formed the change in A is very large due to the large number of very small droplets formed. In order for a microemulsion to be formed (transient) negative value of was required, it is recognized that while value of is positive at all times, it is very small and it is offset by the entropic component[8]. The formulation of microemulsion can be described by following representation,

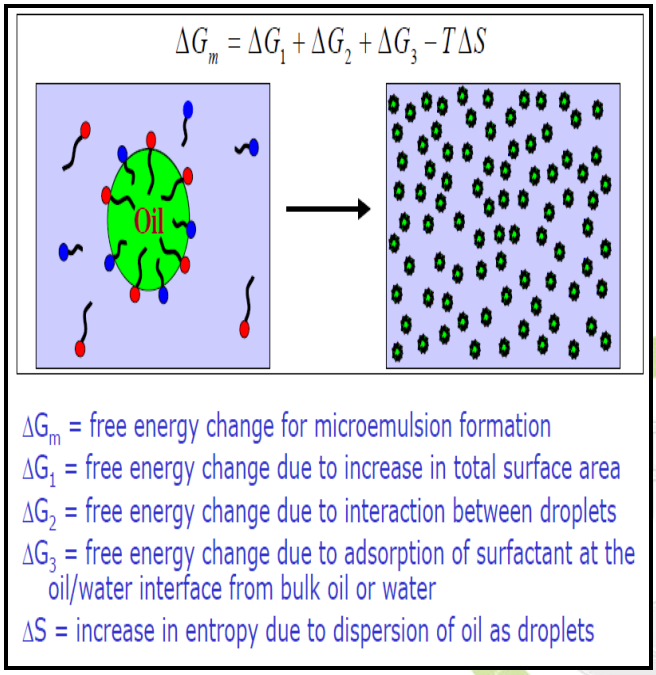

Figure 1: Formation of microemulsion

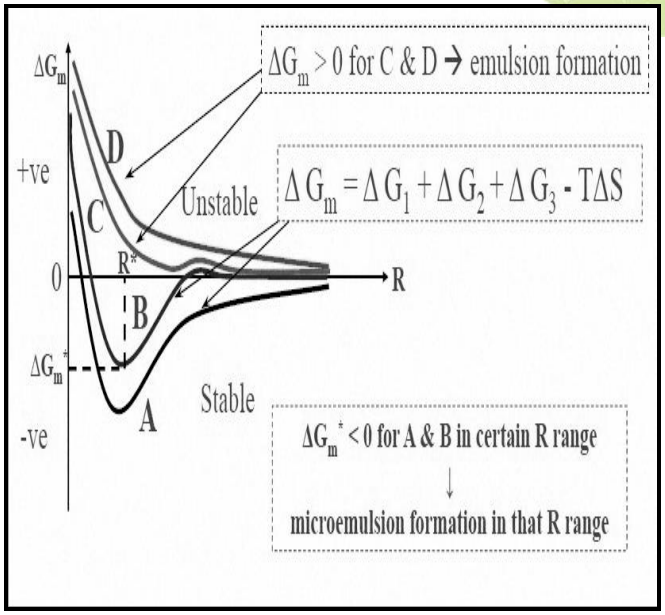

Figure 2: Schematic representations showing the stability of microemulsion

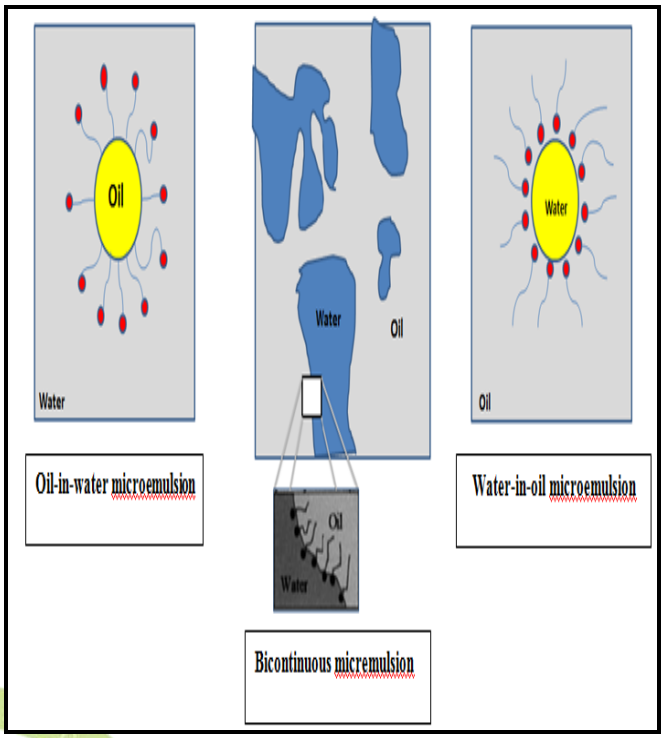

Figure 3: Schematic representations of the three most commonly encountered Microemulsion microstructures: (a) oil-in-water, (b) bicontinuous, and (c) Water-in-oil microemulsion.

Fig. 3 shows schematic representations of the three types of microemulsions which are most likely to form depending on the composition. In the oil-in-water type of microemulsion the fraction of oil is low as compared to water, while in case of water-in-oil the fraction of water is low. Since where the concentration of both oil and water are same, bicontinuous microemulsion occurs in which the oil and water both acts as continuous phase separated by surfactant micelle interface which stabilises the system.

Phase Behaviour Study

The effect of pressure, temperature, concentration on the formation of microemulsion can be illustrated with the help of phase diagram or pseudoternary diagram. This diagram contains triangle of which three corners are represented by water, oil, and surfacten: cosurfactant ratio. Construction of phase diagram is time consuming and not every combination of concentration produce

microemulsion. A series of binary composition is formed and is titrated with the third phase. The end point is determined by careful observation of turbidity and phase separation. A hypothetical phase diagram is shown in figure 4 consist of existing fields with inverse micelle formation in W/O type of microemulsion. From the end point composition of titrated samples, the mass percent composition of the components like oil, surfactant, and water is calculated and is plotted on triangular coordinates to construct pseudoternary phase diagrams.

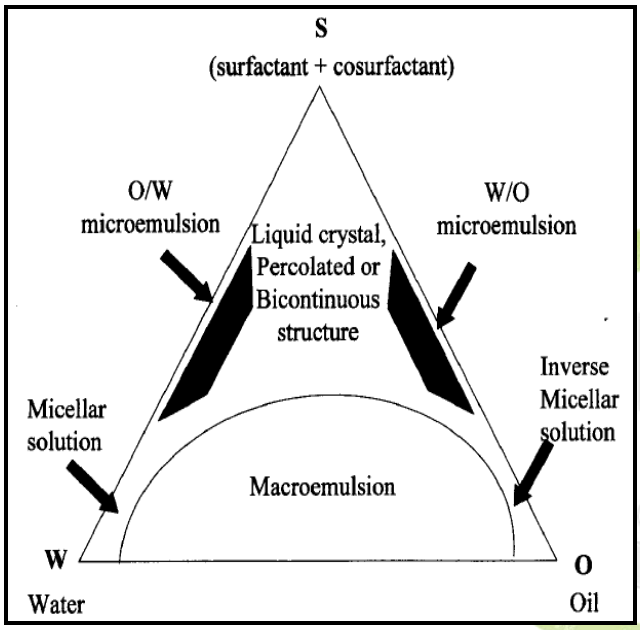

Figure 4: Pseudoternary phase diagram

Each corner of triangle represents the 100% concentration of particular component. In addition to the surfactant, microemulsion contains cosurfactant. The cosurfactant is also strains impose a physical limit on the length of time.

Amphiphilic with an affinity for both the oil and systems can be left to equilibrate and consequently aqueous phases. Cosurfactant mainly contains non ionic surfactant, alcohols, alkyl amines, and alkanediols.

Components of Microemulsion

1. Oil Phase

The selection of oil depends on mainly the solubility of drug. The drug should be highly soluble in oil-surfactant system, since the most of drugs are soluble in the O/W microemulsion. The solubility criteria may enhance the release of drug from system, increases the concentration gradient and enhances the penetration of drug through various biological membranes.

A large number of oils and surfactants are available which can be used as components of microemulsion systems but their toxicity, irritation potential and unclear mechanism of action limit their use. One must choose materials that are biocompatible, non-toxic, clinically acceptable, and use emulsifiers in an appropriate concentration range that will result in mild and non-aggressive microemulsions. The emphasis is, therefore, on the use of generally regarded as safe (GRAS) excipients.

Table 1: the list of various classes and required HLB value

CLASS	Required HLB
Vegetable oils	6
Silicon oil	8-12
Petroleum oil	10
Ester emollients	12
Fatty acids and alcohols	14-15

The oil chain length affects the curvature of monolayer. Increasing the length of oil chain causes more positive curvature which causes the less penetration of surfactant tail region[20].

2. Surfactant[14]

Surfactants are molecules that typically contain a polar head group and an apolar tail. They are surface-active and microstructure-forming molecules with a strong chemical dipole. They are mainly of two types,

- Ionic (cationic or anionic)
- Non ionic (zwitterionic)

The surfactant molecules can arrange themselves in a variety of shapes. They can form spherical micelles, rod-shaped micelles, a

hexagonal phase (consisting of rod-shaped micelles), lamellar (sheet) phases, reverse micelles, or hexagonal reverse micelles.

The hydrophilic-lipophilic balance (HLB) of the surfactant can be taken into account to try to rationalize the surfactant's behaviour. It is generally accepted that a surfactant with HLB from 3-6 will favour the formation of water-in-oil (w/o) microemulsions, where as surfactants with HLB from 8-18 are preferred for oil-in-water (o/w) microemulsions [14].It must be noted, though, that microemulsions are only obtained under certain carefully defined conditions, and the HLB of the surfactant can only be used as a starting point in the selection of components that will form a microemulsion.

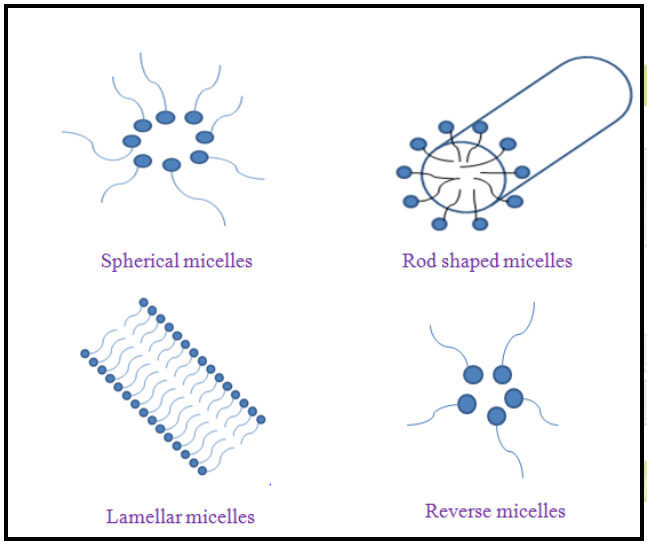

Figure: 5 General Structures of micells formed by surfactants

The concept is to define the surfactant rather than HLB is Critical Packaging Parameter (CPP). The CPP is a measure of the surfactant's preferred geometry, and therefore can be used to predict the type of structure that possibly will be formed. The CPP can be calculated by dividing the partial molar volume of the hydrophobic part of the surfactant by the product of the optimal head group area and length of the surfactant tail. Surfactants that are "cone shaped" where the tail group or head group is much larger than the other will tend to accumulate at curved interfaces resulting in micelles. Surfactants that are more "block shaped" where tail group and head group are similar in size and the CPP values are close to one tend to form worm-like micelles or lamellar structures. Values of CPP greater than one indicate that the head groups are much larger, resulting in w/o microemulsion systems. The opposite is true for CPP values less than one. They generally produce o/w microemulsion systems. Values for CPP around one indicate the possible formation of lamellar phases.

- **Ionic**

Ionic surfactants can be cationic, anionic, or zwitterionic. Cationic surfactants generally fall into the class of quaternary ammonium alkyl salts. Alkyl ammonium halides and tetraalkylammonium halides are the most numerous in this class. Alkyl ammonium halides are excellent hydrogen bond donors and interact strongly with water. The most well known examples from the cationic surfactant class are hexadecyltrimethyl-ammonium bromide (CTAB) and didodcecylammonium bromide (DDAB). Although less numerous, phosphorous can be quaternarized with alkyl groups to create alkyl phosphonium cationic surfactants as well[11]. Dioctyl sodium sulfosuccinate (DOSS) is the most widely studied anionic surfactant. It has twin tails and is a particularly good stabilizer of w/o microemulsions[12].Zwitterionic surfactant contains positive and negative charged groups. Phospholipids, such as lecithin, are common zwitterionic surfactants. They have certain advantages over other surfactants such as biocompatibility, nontoxic.

- **Non ionic**

Non ionic surfactant differs from ionic surfactant as these does not contains any charge and no electrostatic force on the headgroup[11]**.** Ethoxylated alcohols are the most common non ionic surfactants. These alcohols contain a wide-ranging degree of ethoxylation, where ethylene oxide is added to fatty acids to make them more water-soluble. They are considered "amphiphiles", with an oil loving hydrocarbon tail group and water loving ethoxylated alcohol group[13]. Examples of non-ionic surfactants

include polyoxyethylene surfactants, such as Brij 35, or sugar esters, such as sorbitan monooleate (Span 80). Polyoxyethylene sorbitan monooleate (Tween 80) and polyoxyethylene sorbitan monolaurate (Tween 20) appear safe and acceptable for oral and parenteral use[14, 21].

Table 2: A series of non ionic surfactant

HLB	Non ionic surfactant
HLB 2	8% SPAN®80/ 92% SPAN 85
HLB 4	88% SPAN80/ 12% SPAN 85
HLB 6	83% SPAN 80/ 17% TWEEN® 80
HLB 8	65% SPAN 80/ 35% TWEEN 80
HLB 10	46% SPAN 80/ 54% TWEEN 80
HLB 12	28% SPAN 80/ 72% TWEEN 80
HLB 14	9% SPAN 80/ 91% TWEEN 80
HLB 16	60% TWEEN 20 / 40% TWEEN 80

2. Cosurfactant

Sometimes the use of surfactant alone may not lead to the effective formation of microemulsion and microemulsion forming regions. To prepare an optimum microemulsion, sometimes there is need of addition of second surfactant with low molecular weight amphiphile such as alcohol derivatives. Cosurfactants increase the fluidity of hydrocarbon chain of primary surfactants.

Cosurfactants help to further reduce the surface tension and fluidize the surfactant film, which increases the entropy of the system leading to its thermodynamic stability. Co-surfactants increase the flexibility of the surfactant film around the microemulsion droplet. Short and medium chain alcohols, such as butanol, pentanol, ethanol, isopropanol, or propylene glycol, are commonly added as cosurfactants.

But the use of cosurfactant in excess quantity may cause the irritation to the biological system. And uses of some of them are reported as toxic.

The effect cosurfactant on the formation of microemulsion of aminosilicon oil is reviewed. Fig.6A the pseudoternary phase diagram of aminosilicon oil, water, and complex surfactant, shows that to form microemulsion of aminosilicon a high concentration of surfactant is requires. While Fig.6B shows that the use of cosurfactant 1-pentanol is helpful to form a stable and transparent aminosilicon oil microemulsion. Acting a cosurfactant, 1-pentanol can influence the formation of microemulsion by both interfacial and bulk effects[10].

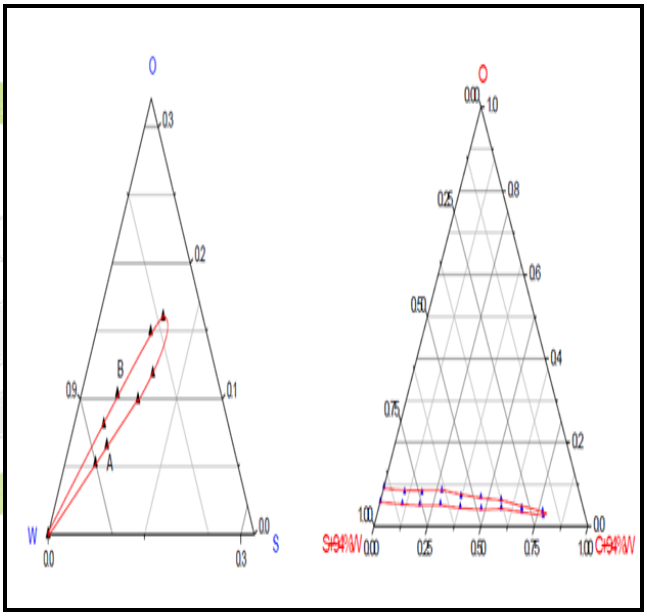

Figure 6: (A) The part pseudo-ternary phase diagram microemulsion aminosilicone oil (O), water (W) and complex surfactants (S) (B) The part pseudo-ternary phase diagram microemulsion aminosilicone oil (O), water (W), complex surfactants (S), and 1-pentanol (C)

Types of Microemulsion[9,17]

Wisnor defined the four general types of microemulsion,

- **Wisnor Type I (O/W):** With two phases, the lower (o/w) microemulsion phases in equilibrium with the upper excess oil.

- **Wisnor Type II (W/O):** With two phases, the upper microemulsion phase (w/o) microemulsion phases in equilibrium with lower excess water
- **Wisnor Type III (B.C.):** With three phases, middle microemulsion phase (o/w plus w/o, called bicontinous) in equilibrium with upper excess oil and lower excess water.
- **Wisnor Type IV (Isotropic micellar solution):** In single phase, with oil, water and surfactant homogenously mixed.

Type I and II are two-phase system while Type III and IV are three-phase system.

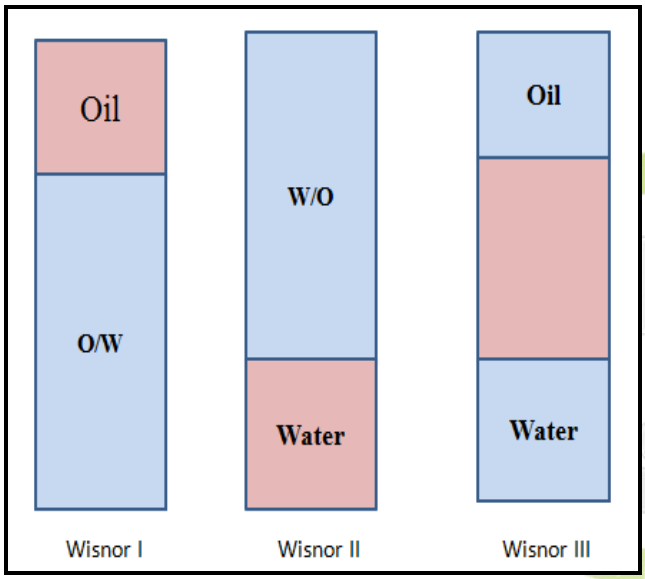

Figure: 7 Types of microemulsion

Interconversions among the above mentioned phases can be achieved by varying the proportions of constituents. Phase transitions are brought about by increasing either electrolyte concentration (in the case of ionic surfactants) or temperature (for non-ionics). Non-ionic surfactants form water−oil microemulsions (and emulsions) with a high temperature sensitivity. In particular, there is a specific phase inversion temperature (PIT) and the film curvature changes from positive to negative. This critical point was defined by Shinoda et al.[18]

Self Microemulsifying Drug Delivery System (SMEDDS)

The principal characteristic of these systems is their ability to form fine oil-in-water (o/w) microemulsions upon mild agitation following dilution by an aqueous phase through the gastrointestinal tract. SMEDDS mainly contains mixture of oil, surfactant, cosurfactant which when administered by oral route get emulsified in stomach Self-emulsifying formulations spread readily in the gastrointestinal (GI) tract, and the digestive motility of the stomach and the intestine provide the agitation necessary for self emulsification. These systems advantageously present the drug in dissolved form and the small droplet size provides a large interfacial area for the drug absorption. When compared with emulsions, which are sensitive and meta-stable dispersed forms, SEDDSs are physically stable formulations that are easy to manufacture. Thus, for lipophilic drug compounds that exhibit dissolution rate-limited absorption, these systems may offer an improvement in the rate and extent of absorption and result in more reproducible blood-time profiles.

Advantages[6]

Potential advantages of these systems (SMEDDS) include,

1. Enhanced oral bioavailability enabling reduction in dose.
2. More consistent temporal profiles of drug absorption.
3. Selective targeting of drug(s) toward specific absorption window in GIT
4. Protection of drug(s) from the hostile environment in gut.
5. Control of delivery profiles.
6. Reduced variability including food effects.
7. Protection of sensitive drug substances.
8. High drug payloads.
9. Liquid or solid dosage forms.

Mechanism of Self Emulsification[5]

According to Reiss, self-emulsification occurs when the entropy change that favours dispersion is greater than the energy required to increase the surface area of the dispersion. The free energy of the conventional emulsion is a direct function of the energy required to create a new surface between the oil and water phases and can be described by the equation:

$$\Delta G = \sum_{i} N_i \pi r_i^2 \sigma$$

Where, DG is the free energy associated with the process (ignoring the free energy of mixing), N is the number of droplets of radius r and s represents the interfacial energy. The two phases of emulsion tend to separate with time to reduce the interfacial area, and subsequently, the emulsion is stabilized by emulsifying agents, who form a monolayer of emulsion droplets, and hence reduces the interfacial energy, as well as providing a barrier to prevent coalescence.

Application

1. Improvement in Solubility and bioavailability

If drug is incorporated in SEDDS, it increases the solubility because it circumvents the dissolution step in case of drug having low solubility and high permeability.

The potential for lipidic self-emulsifying drug delivery systems(SMEDDS) to improve the oral bioavailability of a poorly absorbed, antimalerial drug (Halofantrine, HF) has been investigated in fasted beagles in 1998.The lipid based formulations of HF-base afforded a 6-8 fold improvement in absolute oral bioavailability relative to previous data of the solid HF.

2. Protection Against Biodegradation

Many drugs are degraded in physiological system, may be because of acidic PH in stomach, enzymatic degradation or hydrolytic degradation etc. Such drugs when presented in the form of SEDDS can be well protected against these degradation processes as liquid crystalline phase in SEDDS might be an act as barrier between degradating environment and the drug.

3. Sustain Release

In case of O/W microemulsion, hydrophobic drugs solubilised mainly in the oil droplets, experience hindered diffusion and are therefore released rather slowly (depending on the oil/water partitioning of the substance.

Microemulsion Characterisation

1. Viscosity

Microemulsions are less viscous than conventional emulsion. Measurement of the viscosity is done by Brookfield viscometer. A viscosity measurement is useful in the determination of structure of micells such as rod shaped or reverses micells. This viscosities determination conform whether the system is w/o or o/w. If system has low viscosity then it is o/w type of the system and if a high viscosity then it is w/o type of the system.

2. Conductivity

Conductivity measurements provide a means of determining whether a microemulsion is oil-continuous or water-continuous, as well as providing a means of monitoring percolation or phase inversion phenomena Dielectric measurements are a powerful means of probing both the structural and dynamic features of microemulsion systems.

3. Droplet Size Determination

Size of droplet is measured by photon-correlation spectroscopy (PSC) with Zetasizer. All measurements are carried out at scattering angle of 90° and 25°C temperatures. Prior to measurement, microemulsion is diluted in two-steps with pure water then it is filtered through a 0.22um filter just before it is added to cuvette. In first step it is diluted with equal amount of water. In second step the mixture is further diluted to appropriate concentration for the measurement. That depends on droplet size (Usually diluted 100-200 times).

4. Refractive Index and Percent Transmittance

Refractive index and percent transmittance proved the transparency of formulation. The refractive index of the system is measured by refractometer by placing drop of solution on slide and it compare with water (1.333)**.** The percent transmittance of the system is measured at particular wavelength using UV-spectrophotometer keeping distilled water as blank. If refractive index of system is similar to

the refractive index of water (1.333) and formulation have percent transmittance > 99 percent, then formulation have transparent nature.

5. Permeation Study

Now a day's microemulsion is arising as a topical drug delivery system. Microemulsion enhances the penetration of drug through various biological membranes. The permeation of drug through skin by microemulsion is mainly studied by using various diffusion cells such Franz's diffusion cell, Keshary- chein diffusion cell. For this mainly animal skin is used.

6. Turbidity Measurement

This is to identify efficient selfemulsification by establishing whether the dispersion reaches equilibrium rapidly and in a reproducible time.

Applications of Microemulsion

Microemulsions have shown great potential in the area of pharmaceuticals. They can be applied to a wide variety of dosage forms including oral, topical, ocular, parenteral, periodontal, buccal, and nasal formulations. Oral delivery offers the opportunity to deliver peptide and protein drugs. Usually when peptides and proteins are delivered orally, they are degraded in the GI and are not therapeutically active. Delivery of these molecules using microemulsions, though, increases their bioavailability. The role of microemulsion as a drug delivery system shall be discussed precisely.

Oral Delivery

The oral drug delivery system mainly affected by the stability and solubility of drug. This is challenging aspect for the researchers. Microemulsions have the potential to enhance the solubilisation of the poorly soluble drugs and overcome the dissolution related bioavailability problems. This is particularly important for the BCS class II or class IV drugs. In addition, they can be used for the delivery of hydrophilic drugs including macromolecules such as proteins and peptides. This is due to the existence of polar, nonpolar and interfacial domains which allow encapsulation of drugs with varying solubility. Biowaiver study for BCS Class II drugs by formulation design of cyclosporine self-microemulsifying formulation states that Solubility and dissolution of cyclosporine from SMEDDS were critically enhanced, which were the similar behaviors with BCS class I drug. From this study it is clear that SMEDDS increases the bioavailability of the Class II drugs.

Parenteral Delivery

The formulation of lipophilic and hydrophobic drugs into parenteral dosage forms has proven to be difficult. O/w microemulsions are beneficial in the parenteral delivery of sparingly soluble drugs where the administration of suspension is not desirable. They provide a means of obtaining relatively high concentration of these drugs which usually requires frequent administration. Other advantages are that they exhibit a higher physical stability in plasma than liposomes or other vesicles.

Park KM et al evaluated Flurbiprofen a member of the phenylalkanoic acid derivative family of non- steroidal anti-inflammatory drugs (NSAIDs) used to treat the inflammation and pain, for increasing its solubility by using micremulsion containing ethyl oleate as the oil phase and Tween 20 as surfactant. The maximum solubility of flurbiprofen in the microemulsion system was found to be 10 mg/ml.

Evaluation was done for potential of the microemulsions to improve the parenteral delivery of propofol. Rat paw-lick test indicated that propofol microemulsions were significantly less painful as compared to the marketed propofol formulation. The anaesthetic activity of the microemulsions was similar to the marketed propofol formulation indicating that they do not compromise the pharmacological action of propofol[24].

The preferred anticancer drug Etoposide is also investigated phospholipid-based microemulsion formulation for parenteral delivery. The in vitro erythrocyte toxicity study demonstrated the

safety and acceptability of the formulation for parenteral administration[23].

Topical Application

Topical application the microemulsions can interact with the stratum corneum changing structural rearrangement of its lipid layers and consequently increasing transdermal drug permeation and so act as penetration enhancer. As compared to the conventional vehicle, microemulsion proves to increase the percutanious absorption of drug. Following is the some review of topical microemulsion application,

- **Antifungal**

Topical microemulsions for poorly soluble antifungal agents (miconazole, ketoconazole, and itraconazole) were designed and developed using either mineral oil or olive oil as an oil phase. The release study shown to be increased when compared with gel preparations. The release rates of ketoconazole from microemulsion and gel formulation were 766.8 and 677.6 µg/hour, respectively[1].

Microemulsions of poorly water soluble antifungal drugs miconazole, ketoconazole, and itraconazole were designed and developed by Puranajoti *et al* Various combinations of surfactant ® and cosurfactant were used, including Labrafil M 1944 CS ® ® ® and Plurol Oleique (1:1); Labrafil M 1944 CS and Plurol ® ® Oleique (1:2); or Labrafil M 1944 CS, Capmul MCM C-8, ® Pluro Oleique, and dehydrated ethyl alcohol (3:3:1:1).

A fluconazole w/o microemulsion was developed for topical application using isopropyl myristate as the oil phase and surfactant (tween 80) and co-surfactant (polyethylene glycol 400)[22].

- **Antiviral**

Acyclovir containing microemulsion-based formulations for topical delivery were developed using isopropyl myristate/Captex 355/Labrafac as an oil phase, Tween 20 as surfactent, Span20 as cosurfactant. Transcutol, eucalyptus oil, and peppermint oil were used as permeation enhancers. *In vitro* permeation studies through mice skin were performed using Franz diffusion cells. The optimum formulation containing 2.5% Transcutol as the penetration enhancer showed 1.7-fold enhancement in flux and permeation coefficient as compared to marketed cream and ointment formulation. *In vivo* antiviral studies performed in female mice against induced herpes simplex virus I Infection indicated that a single application of microemulsion formulation containing 2.5% Transcutol, 24 hours post-injection resulted in complete suppression of development of herpetic skin lesions[2]

- **Antiacne**

Microemulsions of azelaic acid, a bioactive molecule used in many skin disorders, prepared using the monosodium salt (AZA-Na) has been evaluated as delivery vehicles. Dialysis membrane experiments showed decreasing permeability to AZA-Na, and this was related to its partition at the microemulsion interface. The results suggested that microemulsions containing AZA-Na could be used to optimize drug targeting in acne treatment[3]

Ophthalmic Delivery

The development and characterisation of o/w microemulsions designed for ocular use has recently been reported. The microemulsions containing pilocarpine were formulated using lecithin, propylene glycol and PEG 200 as cosurfactants, and IPM as the oil phase. The formulations were low viscosity fluids with a refractive index lending them to ophthalmological application. The test microemulsions were non-irritant in rabbit eyes or hen egg membrane.[8]

Pulmonary Delivery

The formulation of a water-in-HFA propellant microemulsion stabilised by fluorocarbon non-ionic surfactant and intended for pulmonary delivery has been described.[24]

Recent Developments in Microemulsion

In concerns with oral delivery of microemulsion recently a pharmacokinetic study with the Sand

immune cyclosporine A Neoral microemulsion concentrate was done showing the improvements in bioavailability and inter / intra-patient variability and was shown to facilitate the effective management of psoriasis[25].

A number of recent reports detail microemulsion formulations designed for topical or transdermal application. Both o/w and a w/o microemulsions have been evaluated in a hairless mouse model for the delivery of prostaglandin E1. The microemulsions were based on oleic acid or Gelucire 44/14 as the oil phase and were stabilized by a mixture of Labrasol (C and C polyglycolysed glycerides) and Plurol Oleique CC 497 as surfactant[26].

Environmentally responsive drug delivery systems are an interesting development and phase changes that occur after administration triggered by changes in temperature, pH or ionic strength can be particularly useful. One example of such behavior involves the phase transformation of a reverse micellar solution of lecithin in IPM to a lamellar liquid crystal. In this case the transition was triggered by contact of the reverse micellar solution with a biological aqueous phase, resulting in the controlled release of the anti-inflammatory fenoprofen[27, 28]. The patent is also issued for the invention of microemulsion containing alkanolammonium salts of alkysulfates and alkypolyyalkyleneglycolethersulfates, UV filters and antidandruff substances. The invention relates to the use of emulsion for cosmetic and medicinal-dermatologic applications[29].

Recently the antimicrobial activity of oil-in-water microemulsion is studied by using test microorganisms (pseudomonas aeruginosa, cadida albicans, Staphylococcus aureus, Aspergillus niger). The results give clear evidence of a good biocidal activity for the microemulsion system against the bacterial species (greater than 6 log cycles of reduction in *P. aeruginosa* viability when exposed to microemulsion Formula 1 in less than 15 s[30].

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