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MICROEMULSIONS: A NOVEL DRUG DELIVERY SYSTEM

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Abstract: The novel carriers have been exploited through almost all the routes of administration. Many newer carriers are evolving in the present time with the advent of technology and the demand of targeted delivery like microemulsions. Microemulsions are clear, stable, isotropic mixtures of oil, water and surfactant, frequently in combination with a cosurfactant. The microemulsion formulations consist of one or more surfactants in combination with co-surfactant and drug dissolved in oil. Oils form a distinct core in the interior of the surfactant aggregate, resulting in enhanced solubilizing capacity of the oils with improved drug loading capacities of the microemulsion. In recent years, numerous studies have suggested that microemulsion [o/w or w/o] as have tremendous potential to enhance the bioavailability of drugs. There the present review focused on microemulsion formulation, advantage and application of microemulsion. Preparing a pharmaceutically acceptable dosage form demands a clear understanding of the micro-emulsion structure, phase behavior, factors leading to its thermodynamic stability, factors influencing drug release from the formulation, requirements of ideal microemulsion excipients, and the potential uses and limitations of the microemulsion system.

Keywords: Microemulsions, Novel carriers, Surfactants, Cosurfactants, Theories, Applications, Advantages.

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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 drugs delivery system has great potential for achieving the goal in drug targeting [1].

The term "microemulsion" refers to a thermodynamically stable, isotropically clear dispersion of two immiscible liquids, such as oil and water, which is stabilized by an interfacial film of surfactant molecules. Surfactant molecules contain both a polar as well as an apolar group. So they exhibit a very peculiar behavior, firstly, they get adsorbed at the interface, where they can fulfill their dual affinity with hydrophilic groups located in aqueous phase and hydrophobic groups in oil or air. Secondly, they reduce mismatching with solvent by Micellization Process. The dispersed phase typically comprises of small particles or droplets, with a size range of 5 nm-200 nm, and has very low oil/water interfacial tension. Because the droplet size is less than 25% of the wavelength of visible light, microemulsions are transparent. The microemulsion is formed readily and sometimes spontaneously, generally without high-energy input. In many cases a cosurfactant or cosolvent is used in addition to the surfactant, the oil phase and the water phase. The concept of 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 today we can adopt the definition given by Attwood: “a microemulsion is a system of water, oil, and amphiphilic compounds (surfactant and co-surfactant) which is a transparent, single optically isotropic, and thermodynamically stable liquid” [2,3,4].

Table.1: Basic Differences between Macroemulsion and Microemulsion [2, 5]

MACROEMULSION	MICROEMULSION
1. It consists of roughly spherical droplets of one phase dispered into the other.	**1.** Microemulsion constantly evolve between various structures ranging from droplet like swollen micelles to bicontinuous structure.
2. Droplet diameter:1-20mm	**2**. Droplet diameter:10-100nm
3. Most emulsions are opaque (white) because of bulk of their droplets is greater than wavelength of light and most oils have higher refractive indices than water.	**3.** Microemlsions are transparent and translucent as their droplet diameter as less than ¼ of the wavelength of light, they scatter little light.

4. Ordinary emulsion droplets, however small exists as individual entities until coalescence or Ostwald ripening occurs.	**4**. Microemulsion droplet may disappear within a fraction of a second whilst another droplet forms spontaneously elsewhere in the system.
5. They may remain stable for long periods of time,will ultimately undergo phase separation on standing to attain a minimum in free energy.They are kinetically stable and thermodynamically unstable.	**5.** More thermodynamically stable than macroemulsion and can have essentially infinite lifetime assuming no change in composition, temperature and pressure and donot tends to separate.
6. They are lyophobic.	**6.** They are on the borderline between lyophobic and lyophillic colloids.
7. They require intense agitation for their formation.	**7.** generally obtained by gentle mixing of ingredients.

Theories of Microemulsion Formation

Historically, three approaches have been used to explain microemulsion formation and stability. They are as follows-

- Interfacial or mixed film theories.
- Solubilization theories.
- Thermodynamic treatments.

The free energy of microemulsion formation can be considered to depend on the extent to which surfactant lowers the surface tension of the oil water interface and change in entropy of the system such that,

Gf = γ a - T S

Where, Gf = free energy of formation

A = change in interfacial area of microemulsion

S = change in entropy of the system

T = temperature

γ = surface tension of oil water interphase

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. The dominant favorable entropic contribution is very large dispersion entropy arising from the mixing of one phase in the other in the form of large number of small droplets. However there are also expected to be favorable entropic contributions arising from other dynamic processes such as surfactant diffusion in the interfacial layer and monomer-micelle surfactant exchange. Thus a negative free energy of formation is achieved when large reductions in surface tension are accompanied by significant favorable entropic change. In such cases, microemulsion is spontaneous and the resulting dispersion is thermodynamically stable [6].

Types of microemulsion systems:

According to Winsor, there are four types of microemulsion phases exists in equilibria, these phases are referred as Winsor phases. They are,

1. Winsor I: With two phases, the lower (o/w) microemulsion phases in equilibrium with the upper excess oil.

2. Winsor II: With two phases, the upper microemulsion phase (w/o) microemulsion phases in equilibrium with lower excess water.

3. Winsor III: With three phases, middle microemulsion phase (o/w plus w/o, called bicontinous) in equilibrium with upper excess oil and lower excess water.

4. Winsor IV: In single phase, with oil, water and surfactant homogenously mixed.

Advantages of microemulsion over other dosage forms

1. Increase the rate of absorption.
2. Eliminates variability in absorption.
3. Helps in solublization of lipophilic drug.
4. Provides a aqueous dosage form for water insoluble drugs.
5. Increases bioavailability.
6. Various routes like tropical, oral and intravenous can be used to deliver the product.
7. Rapid and efficient penetration of the drug moiety.

8. Helpful in taste masking.
9. Provides protection from hydrolysis and oxidation as drug in oil phase in o/w microemulsion is not exposed to attack by water and air.
10. Liquid dosage form increases patient compliance.
11. Less amount of energy requirement [4, 6, 7].

Disadvantages of microemulsion based systems

1. Use of a large concentration of surfactant and co-surfactant necessary for stabilizing nano droplets.

2. Limited solubilizing capacity for high-melting substances.

3. The surfactant must be nontoxic for using pharmaceutical applications.

4. Microemulsion stability is influenced by environmental parameters such as temperature and pH. These parameters change upon microemulsion delivery to patients.

5. For unique dosage preparation in gelatin capsules, it may produce softening or hardening effect on capsule shell, so for long term storage it is undesirable [5, 8].

Components of Microemulsion System

The availability of oils and surfactant is abundance but their use is restricted due to their toxicity, irritation potential and unclear mechanism of action. Oils and surfactant which will be used for the formulation of microemulsion should be biocompatible, non-toxic, and clinically acceptable. The emphasis is on selecting the component which comes under “generally regarded as safe” (GRAS).

A large number of oils and surfactant are available but their use in the microemulsion formulation is restricted due to their toxicity, irritation potential and unclear mechanism of action. Oils and surfactant which will be used for the formulation of microemulsion should be biocompatible, non-toxic, clinically acceptable, and use emulsifiers in an appropriate concentration range that will result in mild and non-aggressive microemulsion. The emphasis is, excipients should be generally regarded as safe (GRAS).

1. Oil phase

2. Aqueous phase

3. Primary surfactant

4. Secondary surfactant (co-surfactant)

5. Co-Solvent

1. Oil phase

Oil is one of the most important components of microemulsion because it can solubilise the required dose of the lipophilic drug and it increases the fraction of lipophilic drug transported via the intestinal lymphatic system. Oil is defined as any liquid having low polarity and low miscibility with water. The examples of such phase are cyclohexane, mineral oil, toulene, & vegetable oil etc.

The oil being one of the most important excipients in the formulation not only because it can solubilise the required dose of the lipophilic drug, it can increase the fraction of lipophilic drug transported via the intestinal lymphatic system, thereby increasing absorption from the GI tract depending on the molecular nature of the triglyceride.

The oil component influences curvature by its ability to penetrate and hence swell the tail group region of the surfactant monolayer. Short chain oils penetrate the tail group region to a greater extent than long chain alkanes, and hence swell this region to a greater extent, resulting in increased negative curvature (and reduced effective HLB).

Following are the different oils are mainly used for the formulation of microemulsion

a. Saturated fatty acid-lauric acid, myristic acid, capric acid.

b. Unsaturated fatty acid-oleic acid, linoleic acid, linolenic acid.

c. Fatty acid ester-ethyl or methyl esters of lauric, myristic and oleic acid.

2. Aqueous phase

Generally the aqueous phase contains hydrophilic active ingredients and preservatives. Sometimes Buffer solutions are used as aqueous phase.

3. Primary surfactant

The surfactant chosen must be able to lower the interfacial tension to a very small value which facilitates dispersion process during the preparation of the microemulsion and provide a flexible film that can readily deform around the droplets and be of the appropriate lipophilic character to provide the correct curvature at the interfacial region. Surfactants used to stabilize microemulsion system may be:

(i) non-ionic,

(ii) zwitterionic,

(iii) cationic, or

(iv) anionic surfactants.

4. Co-surfactants

Cosurfactants are mainly used in microemulsion formulation for following reasons:

- They allow the interfacial film sufficient flexible to take up different curvatures required to form microemulsion over a wide range of composition.
- Short to medium chain length alcohols (C3-C8) reduce the interfacial tension and increase the fluidity of the interface.
- Surfactant having HLB greater than 20 often require the presence of cosurfactant to reduce their effective HLB to a value within the range required for microemulsion formulation.

Following are the different cosurfactant mainly used for microemulsion:

Sorbitan monoleate, sorbitan monosterate, propylene glycol, propylene glycol monocaprylate (Capryol 90), 2-(2-ethoxyethoxy)ethanol (Transcutol) and ethanol.

5. Co-Solvent

The production of an optimum microemulsion requires relatively high concentrations (generally more than 30% w/w) of surfactants. Organic solvents such as, ethanol, propylene glycol (PG), and polyethylene glycol (PEG) are suitable for oral delivery, and they enable the dissolution of large quantities of either the hydrophilic surfactant or the drug in the lipid base. These solvents can even act as co-surfactants in microemulsion systems [1, 4, 5, 6].

Method of preparation

1. Phase titration method

Microemulsions are prepared by spontaneous emulsificationVmethod which is illustrated with help of phase diagrams. Phase diagram construction is practical approach to study complex series of interaction which occurs when different components are mixed. The aspect of the phase diagram is phase equilibrium and demarcation of phase boundaries. Most often pseudo-ternary phase diagrams are constructed to figure out microemulsion zone as quaternary phase diagram is time consuming and difficult to interpret.

2. Phase inversion method

Phase inversion of microemulsion happens upon addition of excess of dispersed phase. Phase inversion leads to radical physical changes as change in particle size that alters drug release. During cooling, this system crosses the point of zero spontaneous curvature and minimal surface tension, prompting the formation of finely dispersed oil droplets. Microemulsions can be prepared by controlled addition of lower alkanols (butanol, pentanol and hexanol) to milky emulsions to produce transparent solutions comprising dispersions of either o/w or w/o or colloidal dispersions. The lower alkanols are called co-surfactants. They lower the interfacial tension between oil and water sufficiently low for almost spontaneous formation [1, 2].

Factors affecting Formulation of Microemulsion System

Property of surfactant

Surfactant contains two group lipophilic and hydrophilic groups. Hydrophilic single chain surfactants such as cetylethyl ammonium bromide dissociate completely in dilute solution and have a tendency to form o/w microemulsion. When the surfactant is in presence of salt or when high concentration of surfactant is used, degree of dissociation of polar groups becomes lesser and resulting system may be w/o type.

Property of Oil Phase

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

Packing Ratio

HLB of surfactant determines the type of microemulsion through its influence on packing and film curvature. The analysis of film curvature for surfactant association`s leading to the formation of microemulsion.

Temperature

Temperature is extremely important in determining the effective head group size of nonionic surfactants. At low temperature, they are hydrophilic and form normal o/w system. At higher temperature, they are lipophilic and form w/o systems. At an intermediate temperature, microemulsion coexists with excess water and oil phases and forms bicontinuous structure.

The Chain Length, Type and Nature of Co-Surfactant:

Alcohols are widely used as a co-surfactant in microemulsions. Addition of shorter chain co-surfactant gives positive curvature effect as alcohol swells the head region more than tail region so, it becomes more hydrophilic and o/w type is favoured, while longer chain co-surfactant favours w/o type w/o type by alcohol swelling more in chain region than head region [1, 5].

Characterization of Microemulsions

Microemulsions have been characterized using a wide variety of techniques. The characterization of microemulsions is a difficult task due to their complexity, variety of structures and components involved in these systems, as well as the limitations associated with each technique but such knowledge is essential for their successful commercial exploitation. Therefore, complementary studies using a combination of techniques are usually required to obtain a comprehensive view of the physicochemical properties and structure of microemulsions. At the macroscopic level viscosity, conductivity and dielectric methods provides useful information.

(A) Phase Behavior Studies

Phase behavior studies are essential for the study of surfactant system determined by using phase diagram that provide information on the boundaries of the different phases as a function of composition variables and temperatures, and, more important, structural organization can be also inferred. Phase behaviour studies also allow comparison of the efficiency of different surfactants for a given application. In the phase behaviour studies, simple measurement and equipments are required. The boundaries of one-phase region can be assessed easily by visual observation of samples of known composition. The main drawback is long equilibrium time required for multiphase region, especially if liquid crystalline phase is involved.

Other useful means and ways of representing the phase behaviour are to keep the concentration of one component or the ratio of two components constant. As the number of components increases, the number of experiments needed to define the complete phase behaviour becomes extraordinary large and the representation of phase behaviour becomes extremely complex. One approach to characterize these multicomponent systems is by means of pseudo-ternary diagrams that combine more than one component in the vertices of the ternary diagram.

(B) Scattering Techniques for Microemulsion Characteruzation

Small-angle X-ray scattering (SAXS), small-angle neutron scattering (SANS), and static as well as dynamic light scattering are widely applied techniques in the study of microemulsions. These methods are very valuable for obtaining quantitative informations on the size, shape and dynamics of the components. The major drawback of this technique is the dilution of the sample required for the reduction of interparticular interaction. This dilution can modify the structure and the composition of the pseudophases. Nevertheless, successful determinations have been carried out using a dilution technique that maintains the identity of droplets. Small-angle X-ray scattering techniques have been used to obtain information on droplet size and shape. Static light scattering techniques have also been widely used to determine microemulsion droplet size and shape. In these experiments the intensity of scattered light is generally measured at various angles and for different concentrations of microemulsion droplets. Dynamic light scattering, which is also referred as photon correlation spectroscopy (PCS), is used to analyse the fluctuations in the intensity of scattering by the droplets due to Brownian motion. The self-correlation is measured that gives information on dynamics of the system.

(C) Nuclear Magnetic Resonance Studies The structure and dynamics of microemulsions can be studied by using nuclear magnetic resonance techniques. Self-diffusion measurements using different tracer techniques, generally radio labeling, supply information on the mobility of the components. 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 (in the range of 10^{-9} to 10^{-12} m^2s^{-1}), of many components.

(D) Interfacial Tension The formation and the properties of microemulsion can be studied by measuring the interfacial tension. Ultra low values of interfacial tension are correlated with phase behaviour, particularly the existence of surfactant phase or middle-phase microemulsions in equilibrium with aqueous and oil phases. Spinning-drop apparatus can be used to measure the ultra low interfacial tension. Interfacial tensions are derived from the

measurement of the shape of a drop of the low-density phase, rotating it in cylindrical capillary filled with high-density phase.

(E) Viscosity Measurements Viscosity measurements can indicate the presence of rod-like or worm-like reverse micelle. Viscosity measurements as a function of volume fraction have been used to determine the hydrodynamic radius of droplets, as well as interaction between droplets and deviations from spherical shape by fitting the results to appropriate models (e.g. for microemulsions showing Newtonian behaviour, Einstein's equation for the relative viscosity can be used to calculate the hydrodynamic volume of the particles).

(F) Simple tests

Dye Solubilization A water soluble dye is solubilized within the aqueous phase of the W/O globule but is dispersible in the O/W globule. A oil soluble dye is solubilized within the oil phase of the O/W globule but is dispersible in the W/O globule.

Dilutability Test O/W microemulsions are dilutable with water whereas W/O are not and undergo phase inversion into O/W microemulsion.

Conductance Measurement O/W microemulsion where the external phase is water are highly conducting whereas W/O are not, since water is the internal or dispersal phase. To determine the nature of continuous phase and to detect phase inversion phenomena, the electrical conductivity measurements are highly useful. A sharp increase in conductivity in certain W/O microemulsion systems was observed at low volume fractions and such behaviour was interpreted as an indication of a 'percolative behaviour' or exchange of ions between droplets before the formation of bicontinuous structures. Dielectric constants are a powerful means of probing both structural and dynamic features of microemulsions systems.

(G) Electron Microscope Characterization

Transmission Electron Microscopy (TEM) is the most important technique to study of microstructures of microemulsions. There are two variations of TEM technique for fluid samples.

1. The cryo-TEM analyzes in which samples are directly visualized after fast freeze and freeze fructose in the cold microscope.

2. The Freeze Fracture TEM technique in which a replica of specimen is images under specified conditions.

(H) Stability Studies The stability of the microemulsion has been assessed by conducting long term stability study and accelerated stability studies. In long term stability study, the system is

kept at room temperature, refrigeration temperature (4-8 ˚C) and elevated temperature (50±2 ˚C). Over the time period, microemulsion systems are evaluated for their size, zeta potential, assay, pH, viscosity and conductivity. On long term study, the activation energy for the system and shelf life of the system may be calculated as like other conventional delivery system. Accelerated stability studies are the essential tools to study the thermodynamic stability of microemulsions. It can be done by centrifugation, heating/cooling cycle and freeze/thaw cycles [2, 6, 8].

Applications of Microemulsion

Microemulsion in pharmaceuticals

Parenteral administration: Parenteral administration (especially via the intravenous route) of drugs with limited solubility is a major problem in the pharmaceutical industry because of the extremely low amount of drug actually delivered to a targeted site. Microemulsion formulations have distinct advantages over macroemulsion systems when delivered parenterally because of the fine particle, microemulsion 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 microemulsion can be used for parenteral delivery.

Oral administration: Oral administration of microemulsion formulations offer several benefits over conventional oral formulation including increased absorption, improved clinical potency, and decreased drug toxicity. Therefore, microemulsion has been reported to be an ideal delivery of drugs such as steroids, hormones, diuretic and antibiotics.

Pharmaceutical drugs of peptides and proteins are highly potent and specific in their physiological functions. However, most are difficult to administer orally. With on oral bioavailability in conventional (i.e. non-microemulsion 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 by parenteral route, so require multiple dosing .

a. **Topical administration:** Topical administration of drugs can have advantages over other methods for several reasons, one of which is the avoidance of hepatic first pass metabolism of the drug and related toxicity effects. Another is the direct delivery and targetability of the drug to the affected area of the skin or eyes.

b. **Ocular and pulmonary delivery:** Ocular and pulmonary delivery for the treatment of eye diseases, drugs are essentially delivered topically. O/W microemulsions have been

investigated for ocular administration, to dissolve poorly soluble drugs, to increase absorption and to attain prolong release profile.

Microemulsions in biotechnology

Many enzymatic and biocatalytic reactions are conducted in pure organic or aqua-organic media. Biphasic media are also used for these types of reactions. The use of a pure polar media causes the denaturation of biocatalysts. The use of water-proof media is relatively advantageous. Enzymes in low water content display and have:

1. Increased solubility in non-polar reactants.

2. Possibility of shifting thermodynamic equilibrium in favour of condensations.

3. Improvement of thermal stability of the enzymes, enabling reactions to be carried out at higher temperatures.

Many enzymes, including lipases, esterases, dehydrogenases and oxidases often function in the cells in microenvironments that are hydrophobic in nature. In biological systems many enzymes operate at the interface between hydrophobic and hydrophilic domains and these usually interfaces are stabilized by polar lipids and other natural amphiphiles. Enzymatic catalysis in microemulsions has been used for a variety of reactions, such as synthesis of esters, peptides and sugar acetals transesterification; various hydrolysis reactions and steroid transformation. The most widely used class of enzymes in microemulsion-based reactions is of lipases.

Solubilization of drug in microemulsion

Microemulsion possesses interesting physicochemical properties, i.e. transparency, low viscosity, thermodynamic stability, high solubilization power. Because of these specific properties of microemulsion can be useful as a drug delivery system. Different categories of drugs can be solubilized in microemulsion systems for their better therapeutic efficacy.

Microemulsions as coatings and textile finishing

The coating application area is a very promising and rapidly-growing field of microemulsion technology, because the microemulsified resins overcome many of the shortcomings of the more traditional water-based systems without creating the health and pollution problems and flammability hazards of the solvent-based coatings. Due to their stability and small droplet size, microemulsions are ideal, where stability and homogeneity of the finished product is desired. Paint formulations using microemulsions have shown higher scrub resistance, better colour intensity and more stain resistance than those prepared by emulsions.

In principle, three different possibilities of using microemulsions exist for coating applications: (1) for producing microdispersions by using microemulsified monomers,

(2) for transferring non-water-soluble polymers into water,

(3) for obtaining specific effects by polymerization in w/o system.

A microemulsion as fuels

A microemulsion-based fuel in the presence of water is one of the advantages of stable microemulsion and they are successfully used to reduce soot formation. When the water is vaporized during the combustion, this will lower the heat released and the combustion temperature. As a direct consequence, the emission rate of gases like nitrogen oxides (NOx) and carbon monoxide (CO) will decrease.

The presence of water is also supposed to cause improved fuel atomization, minimization of particulate emission and sooting, and improved fuel economy in terms of price and miles/volume of the fuel. Another interesting feature of microemulsion-based fuel is their capacity to increase the octane number of gasoline and the corresponding octane number for diesel oils. Octane number improvers include formamide, glycols, urea, etc. In diesel fuels, many problems are overcome due to the high combustion temperatures (160–325°C). It is normal that diesel microemulsions contain water soluble cetane number improvers.

Microemulsions as lubricants, cutting oils and corrosion inhibitors

Microemulsions or reverse micellar solutions are in use as lubricants, cutting oils and corrosion inhibitors for several decades. The presence of surfactant in microemulsion causes corrosion inhibition and the increased water content compared to pure oil leads to higher heat capacity. On one hand the corrosive agents, because of solubilization in microemulsion cannot react with the metal surface and on the other, the metal surface is protected by the adsorbed hydrophobic surfactant film. However, solubilization is selective, and in some cases, other mechanisms might play a role in corrosion prevention. In microemulsions, water with much higher thermal conductivity, imparts higher heat capacity to the system. Such formulations can be used in cutting oil; the oil lubricates the cutting surface, and the water helps to remove the frictional heat generated during the cutting process.

Microemulsions in cosmetics

In many cosmetic applications such as skin care products, emulsions are widely used with water as the continuous phase. It is believed that microemulsion 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.

Unique microemulsions as hair care products have been prepared. They contain an amino-functional polyorganosiloxane (a nonionic surfactant) and an acid and/or a metal salt. Solubilization of fragrance and flavored oils can be achieved in microemulsions. Cosmetic microemulsions (transparent and translucent) of silicone oils, produced by emulsion polymerization have been reported. They are, however, not thermodynamically stable products because of low solubility of silicone oil in the surfactants. Ultra fine emulsions prepared by condensation method have some advantages in cosmetic and medical products, as they have excellent stability and safety and their droplet size can be readily controlled. Ultrafine emulsions can be regarded as thermodynamically unstable microemulsions, as they are O/W emulsions with droplet size similar to microemulsion. Cosmetic formulations for skin care products using commercial nonionic surfactants and oils usually used in cosmetics are also investigated.

Microemulsions in food

Certain foods contain natural microemulsions. Microemulsions as a functional state of lipids have been, therefore, used in the preparation of foods. Microemulsions form in the intestine during the digestion and absorption of fat. The possibility of producing microemulsion on purpose and using them as tools in food production is, however, a neglected field in food technology. Excellent component solubilization, enriched reaction efficiency and extraction techniques have considerable potential in the area of food technology. An important application of microemulsion is to provide improved antioxidation effectiveness because of the possibility of a synergistic effect between hydrophilic and lipophilic antioxidants. It is known that soybean oil is effectively protected when contained within an L2- phase produced by the addition of monoglycerides (sunflower oil monoglycerides) to water. An approximately 1:5 ratio of monoglycerides to triglycerides is needed to get enough water into the L2-phase (about 5 wt %). In such a system, 200 ppm of tocopherol in the oil and 5% ascorbic acid in the reverse micelles give a dramatic antioxidant effect compared to conventional methods of dissolving or dispersing antioxidants in oils. In fish oils, the same microemulsion-based method to achieve an antioxidant protective effect has also been used. Glycerol has been used instead of water for further improvement of the protectivity [1, 4, 6, 7, 8].

Table. 2: Research work carried out on Microemulsions Drug Delivery System [1, 2, 9-14]

S.No.	Drug	Category	Route
1.	Fluconazole	Antifungal	Topical
2.	Piroxicam	NSAID	Topical
3.	Acyclovir	Antiviral	Topical
4.	Aceclofenac	NSAID	Percutaneous
5.	Ketorolac tromethamine	NSAID	Topical
6.	Celecoxib	NSAID	Topical
7.	Sertaconazole	Antifungal	Topical
8.	Diclofenac Sodium	NSAID	Transdermal
9.	Clotrimazole	Antifungal	Vaginal
10.	Fexofenadine	Antihistamines	Oral
11.	Lorazepam	Antiepileptic	Parenteral
12.	Clopidogrel	Antiplatelet	Oral
13.	Flurbiprofen	Analgesics	Parenteral
14.	Apomorphine Hcl	Antiparkinson	Transdermal
15.	Ketoprofen	Analgesics	Transdermal
16.	Fenofibrate	Antihyperlipidemic	Self micro emulsifying
17.	Estradiol	Anticholesteremic	Transdermal
18.	Timolol	Antihypertensive	Opthalmic
19.	Ibuprofen	Analgesic	Parenteral
20.	Piroxicam	Cyclooxygenase Inhibitors	Oral
21.	Progesterone	Hormones	Dermal
22.	Terbinafine	Antifungal	Transdermal
23.	Amphotericin	Antifungal	Parenteral
24.	Dexamethasone	Glucocorticoids	Topical ocular
25.	Itraconazole	Antifungal	Parenteral
26.	Prilocaine Hcl	Local Anesthetics	Transdermal
27.	Chloramphenicol	Antibacterial	Ocular
28.	Olanzapine	Antipsychotic	Intranasal
29.	Sertraline hydrochloride	Selective Serotonin reuptake inhibitor	Intranasal
30.	Isotretinoin	Retinoids	Oral
31.	Pitavastatin	Statins	Oral
32.	Vitamin A Palmitate	Vitamins	Oral
33.	Famotidine	Antiulcer	Oral

Table. 3: Microemulsion based marketed product [1, 2]

S. No.	Brand Name	Composition	Manufactured By
1.	Sandimmune Neoral®	Cyclosporin A	Novartis
2.	Norvir ®	Ritonavir	Roche laboratories
3.	White Glow	Mulberry Extract	Lotus Herbals
4.	Fortovase ®	Saquinavi	Roche laboratories

CONCLUSION

In the recent years microemulsions came as a attention making novel drug delivery system because of their importance in industrial application. During the last two decades lot of research work has been carried out on microemulsion system for providing novel solutions to overcome the problems of poor aqueous solubility of highly lipophilic drug compounds and provide reproducible bioavailability. Microemulsion can also be used for cosmetic purpose and drug targeting. Now a day, researcher work is focused on the production of safe, efficient and more compatible microemulsion constituents which will further enhance the utility of this novel delivery system. There is still a considerable amount of fundamental work characterizing the physico-chemical behaviors of microemulsions that need to be performed before they can live to their potential as multipurpose drug delivery vehicle.

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