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Microemulsions: A Novel Approach to Enhanced Drug Delivery

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ABSTRACT: Microemulsions are excellent candidates as potential drug delivery systems because of their improved drug solubilization, long shelf life, and ease of preparation and administration. The formulation of microemulsion for pharmaceutical use requires a thorough understanding of the properties, uses, and limitations of microemulsion. Three distinct microemulsions – oil external, water external and middle phase can be used for drug delivery, depending upon the type of drug delivery upon the type of drug and the site of action. In this article, Since the term 'microemulsion' was first coined almost fifty years ago to describe clear, isotropic, thermodynamically stable systems composed of oil, water, surfactant and cosurfactant, numerous and varied reports of the applications of microemulsions have appeared in the literature. Reports of the use of microemulsions in separation science began to appear in the literature in the early 1990's when they were first used as mobile phases for HPLC and as carrier electrolytes for CE separations, particularly for pharmaceutical applications.

KEYWORDS: Microemulsions, Micelle, Thermodynamics, Co-solvents, Transparent, Coarse.

I. INTRODUCTION

The term "microemulsion" refers to a thermodynamically stable isotropically clear dispersion of two immiscible liquids, such as oil and water, stabilized by an interfacial film of surfactant molecules. A microemulsion is considered to be a thermodynamically or kinetically stable liquid dispersion of an oil phase and a water phase, in combination with a surfactant. The dispersed phase typically comprises 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.
Three types of microemulsions are most likely to be formed depending on the composition:

- Oil in water microemulsions wherein oil droplets are dispersed in the continuos aqueous phase
- Water in oil microemulsions wherein water droplets are dispersed in the continuous oil phase;
- Bi-continuous microemulsions wherein microdomains of oil and water are interdispersed within the system.

In all three types of microemulsions, the interface is stabilized by an appropriate combination of surfactants and/or co-surfactants.

A. HISTORY

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.(1)

The existence of this theoretical structure was later confirmed by use of various technologies, and we can today 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)

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B. OBJECTIVES

The overall objective of this thesis was to develop stable salt-containing w/o microemulsions for possible release applications. The specific objectives were:

1. To prepare and optimise w/o microemulsions using combinations of surfactants, organic and aqueous phases and to characterise the resulting microemulsions along two dilution lines within the monophasic region in ternary phase diagrams.
2. To incorporate a model hydrophilic guest molecule (sodium chloride) into the water domains of oil-continuous microemulsions and to characterise these salt containing microemulsions along the two dilution lines within the monophasic regionin developed tertiary phase diagrams.
3. To test the efficiency of selected salt-containing microemulsion compositions for salt-release using conductivity and establish the mechanism of release.

C. FORMULATION

Microemulsions are colloidal dispersions composed of an oil phase, aqueous phase, surfactant and cosurfactant at appropriate ratios.

Unlike coarse emulsions micronized with external energy microemulsions are based on low interfacial tension. This is achieved by adding a cosurfactant, which leads to spontaneous formation of a thermodynamically stable microemulsion.

The droplet size in the dispersed phase is very small, usually below 140 nm in diameter, which makes the microemulsions transparent liquids.[3] In principle, microemulsions can be used to deliver drugs to the patients via several routes, but the topical application of microemulsions has gained increasing interest.

A unique attempt was made[4] of emulsify coconut oil with the help of polyoxyethylene 2-cetyl ether (Brij 52) and isopropanol or ethanol, forming stable isotropic dispersion thus paving way for use of plant and vegetable oil to be used as oil phase in microemulsion.

The surfactants used to stabilise such systems may be:

(i) Non-ionic
(ii) Zwitterionic
(iii) Cationic
(iv) Anionic surfactants

A combinations of these, particularly ionic and non-ionic, can be very effective at increasing the extent of the microemulsion region.

- Non-ionics include polyoxyethylene surfactants such as Brij 35 (C12E35) or a sugar esters such as sorbitanmonooleate (Span 80). Phospholipids are a notable.
- Zwitterionic surfactants and exhibit excellent biocompatibility. Lecithin preparations from a variety of sources including soybean and egg are available commercially and contain diacylphosphatidylcholine as its major constituent.[5-8]
- Cationic surfactants: Quaternary ammonium alkyl salts form with hexadecyltrimethyl ammonium bromide (CTAB), and the twin-tailed surfactant didodcecylammonium bromide (DDAB) are amongst the most well known.
- Anionic surfactan: The most widely studied is probably sodium bis-2-ethylhexylsulphosuccinate (AOT) which is twin-tailed and is a particularly effective stabiliser of w/o microemulsions.[9]

Attempts have been made to rationalise surfactant behaviour in terms of the hydrophile–lipophile balance (HLB)[10], as well as the critical packing parameter (CPP).[11,12]Both approaches are fairly empirical but can be a useful guide to surfactant selection. The HLB takes into account the relative contribution of hydrophilic and hydrophobic fragments of the surfactant molecule. It is generally accepted that low HLB (3–6) surfactants are favoured for the formation of w/o microemulsions whereas surfactants with high HLBs (8–18) are preferred for the formation of o/w microemulsion systems. Ionic surfactants such as sodium dodecyl sulphate which have HLBs greater than 20, often require the presence of a cosurfactant to reduce their effective HLB to a value within the range required for microemulsion

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formation. In contrast, the CPP relates the ability of surfactant to form particular aggregates to the geometry of the molecule itself.
In most cases, single-chain surfactants alone are unable to reduce the oil /water interfacial tension sufficiently to enable a microemulsion to form, a point made in a number of pertinent microemulsions reviews.[13-17] Medium chain length alcohols which are commonly added as cosurfactants, have the effect of further reducing the interfacial tension, whilst increasing the fluidity of the interface thereby increasing the entropy of the system.[14, 15] Medium chain length alcohols also increase the mobility of the hydrocarbon tail and also allow greater penetration of the oil into this region.Various pharmaceutically acceptable excipients available that can be used in microemulsion formulation are:

D. PREPARATION OF MICROEMULSION

The drug is be dissolved in the lipophilic part of the microemulsion i.e. Oil and the water phases can be combined with surfactant and a cosurfactant is then added at slow rate with gradual stirring until the system is transparent. The amount of surfactant and cosurfactant to be added and the percent of oil phase that can be incorporated shall be determined with the help of pseudoternary phase diagram. Ultrasonicator can finally be used so to achieve the desired size range for dispersed globules. It is then be allowed to equilibrate.
Gel may be prepared by adding a gelling agent to the above microemulsion. Carbomers (crosslinkedpolyacrylic acid polymers) are the most widely used gelling agent.

E. CONSTRUCTION OF PHASE DIAGRAM:

Pseudo-ternary phase diagrams of oil, water, and cosurfactant/surfactants mixtures are constructed at fixed cosurfactant/surfactant weight ratios. Phase diagrams are obtained by mixing of the ingredients, which shall be preweighed into glass vials and titrated with water and stirred well at room temperature. Formation of monophasic/ biphasic system is confirmed by visual inspection. In case turbidity appears followed by a phase separation, the samples shall be considered as biphasic. In case monophasic, clear and transparent mixtures are visualized after stirring, the samples shall be marked as points in the phase diagram. The area covered by these points is considered as the microemulsion region of existence.

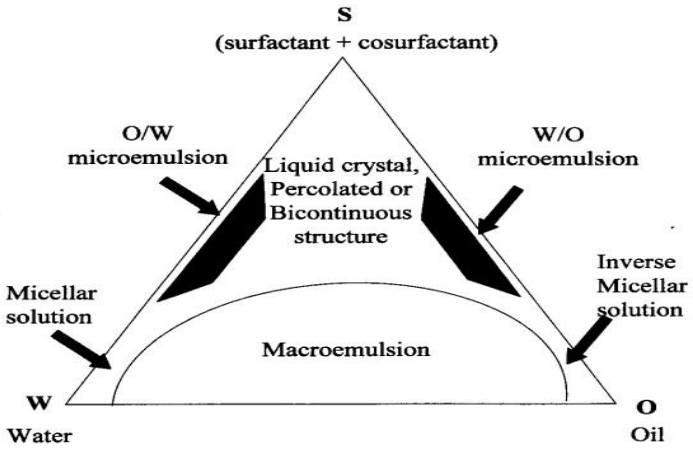

Figure 1: Hypothetical phase regions of microemulsion system of oil (O), water (W), and surfactant + cosurfactant (S)

F. CHARACTERIZATION OF MICROEMULSION:

The droplet size, viscosity, density, turbidity, refractive index, phase separation and pH measurements shall be performed to characterize the microemulsion.
The droplet size distribution of microemulsion vesicles can be determined by either light scattering technique or electron microscopy. This technique has been advocated as the best method for predicting microemulsion stability.

G. ADVANTAGES OF MICROEMULSION OVER OTHER DOSAGE FORMS:

- Increase the rate of absorption

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- Eliminates variability in absorption
- Helps solublize lipophilic drug
- Provides a aqueous dosage form for water insoluble drugs
- Increases bioavailability
- Various routes like tropical, oral and intravenous can be used to deliver the product
- Rapid and efficient penetration of the drug moiety
- Helpful in taste masking
- Provides protection from hydrolysis and oxidation as drug in oil phase in O/W microemulsion is not exposed to attack by water and air.
- Liquid dosage form increases patient compliance.

- Less amount of energy requirement.

H. DIFFERENCES BETWEEN EMULSION &MICROEMULSION:

In contrast to ordinary emulsions, microemulsions form upon simple mixing of the components and do not require the high shear conditions generally used in the formation of ordinary emulsions. The two basic types of microemulsions are direct (oil dispersed in water, o/w) and reversed (water dispersed in oil, w/o).

The main difference between emulsions and microemulsions is in the size and shape of the droplets that are dispersed in the continuous phase, reflecting the differences in the thermodynamic stability of the two systems (Table 1). Emulsions are kinetically stable but thermodynamically unstable, and after storage oraging, droplets will coalesce and the two phases separate. In contrast, microemulsions are thermodynamically stable and will not separate into the corresponding phases. It should be stressed that the term "mini-emulsions" was coined by some authors to describe emulsion droplets of submicron size with improved stabilities, other scientists may call those emulsions "nanoemulsions." While nanoemulsions do not have a long shelf life, they frequently are freshly prepared and used. It should also be stressed that in some studies, the authors neglect to test stability and consider mini- or nanoemulsions to be true microemulsions. The kinetics of microemulsion polymerization has much in common with emulsion polymerization kinetics, the most characteristic feature of which is the compartmentalization, where the radicals growing inside the particles are separated from each other, thus suppressing termination to a high extent and, as a consequence, providing high rates of polymerization.

Microemulsions can be sterilized by filtration and their production is relatively simple and inexpensive. Because of these properties, they have attracted a great interest as drug

Delivery vehicle [17,18]Microemulsions can be applied as liquid membrane carriers to transport lipophilic substances through an aqueous medium or to carry hydrophilic substances across lipoidal medium. They are proposed for oral, topical, dermal, transdermal, parentenal and pulmonary administration of drugs[19] Although microemulsions have been known for a long period, their potential as vehicles for topical ocular drug delivery has been investigated only within the last decade[20] The main problem in a microemulsion application is a high concentration and a narrow range of physiologically

acceptable surfactants and co-surfactants. [21,22]. On the other hand, the large surfactant concentration determines their stability.

Factors Affecting the Microemulsion:

The formation of microemulsion will depend on the following factors

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- **Packing ratio**: The HLB of surfactant determines the type of microemulsion through its influence on molecular packing and film curvature. The analysis of film curvature for surfactant association's leadings to the formation of microemulsion.
- **Property of surfactant, oil phase and temperature**: The type of microemulsion depends on the nature of surfactant. Surfactant contains hydrophilic head group and lipophilic tail group. The areas of these group,

Properties	Emulsions		Microemulsions
	Miniemulsion	Macroemulsion	NSSL
Visual aspect			
Typical characteristic size	20–200nm	>1 µm	10–100nm
Stability	Kinetic		Thermodynamic
Formation	Energy input		Spontaneous
Surfactant concentration	Low		High

Table 1: Difference between miniemulsion, macroemulsion and microemulsion.

which are a measure of the differential tendency of water to swell head group and oil to swell the tail area are important for specific formulation when estimating the surfactant HLB in a particular system. When a high concentration of the surfactant is used or when the surfactant is in presence of salt, degree of dissociation of polar groups becomes lesser and resulting system may be w/o type. Diluting with water may increase dissociation and leads to an o/w system. Ionic surfactants are strongly influenced by temperature. It mainly causes increased surfactant counterion dissociation. The oil component also influences curvature by its ability to penetrate and hence swell the tail group region of the surfactant monolayer. Short chains oils penetrate the lipophilic group region to a great extent and results in increased negative curvature. 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 cosurfactant: Alcohols are widely used as a cosurfactant in microemulsions. Addition of shorter chain cosurfactant 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 cosurfactant favours w/o type w/o type by alcohol swelling more in chain region than head region.

I. EVALUATION / CHARACTERIZATION OF MICROEMULSION:

The microemulsions are evaluated by the following techniques. They are

(I) ***Phase behavior studies:*** visual observations, phase contrast microscopy and freeze fracture transmission electron microscopy can be used to differentiate microemulsions and coarse emulsions. Clear isotropic one-phase systems are identified as microemulsions whereas opaque systems showing bifringence when viewed by cross polarized light microscopy may be taken as liquid crystalline system.

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II)Scattering Techniques: Scattering techniques such assmall angle neutron scattering, small angle X-ray scattering and light scattering have found applications in studies of microemulsion structure, particularly in case of dilute monodisperese spheres, when polydisperse and/or concentrated systems such as those frequently seen in microemulsions.

(III) Transmittance test

Stability of the optimized microemulsion formulation with respect to dilution was checked by measuring transmittance at a specific wavelength with a UV spectrophotometer .

(IV) Globule size and zeta potential measurements

The globule size and zeta potential of themicroemulsion can be determined by dynamic light scattering, using a Zetasizer HSA 3000.

(V) Viscosity measurements

Rheological behavior of the formulation can be observed by using a Brookfield LVDV III+ cone and plate (CP) viscometer (Mfg: Brookfield, USA) using rheocal software at a temperature.Change in the rheological characteristics help in determining the microemulsion region and its separation from other region. Bicontinuousmicroemulsion are dynamic structures with continuous fluctuations occurring between the bicontinuous structure, swollen reverse micelle, and swollen micelles

(VI) Electrical conductivity

The water phase was added drop wise to a mixture of oil, surfactant and co-surfactant and the electrical conductivity of formulated samples can be measured using a conductometer (CM 180 conductivity meter, Elico, India) at ambient temperature and at a constant frequency of 1 Hz.

(VII) Drug stability

The optimized microemulsion was kept under cold condition (4-8 ^{o}C), room temperature and at elevated temperature (50 ± 2 ^{o}C). After every 2 months the microemulsion can be analyzed for phase separation, % transmittance, globule size and % assay.

(VIII) Drug solubility

Drug was added in excess to the optimized microemulsion formulation as well as each individual ingredient of the formulation. After continuous stirring for 24 h at room temperature, samples were withdrawn and centrifuged at 6000 rpm for 10 min. The amount of soluble drug in the optimized formulation as well as each individual ingredient of the formulation was calculated by subtracting the drug present in the sediment from the total amount of drug added. The solubility of drug in microemulsion was compared with respect to its individual ingredients.

(IX)Drug release studies (A) In-vitro drug release

The diffusion study can be carried out on a modified Franz diffusion cell, within volume of 20mL. The receptor compartment was filled with of buffer .The donor compartment was fixed with cellophane membrane , containing the microemulsion formulation and the plain drug solution, separately. At predetermined time intervals samples were withdrawn from the receptor compartment and analyzed for drug content, using a UV spectrophotometer at specific wavelength.

(B) Ex-vivo drug release

Ex -vivo drug release into buffer was studied using intestinal membrane within a Franz diffusion cell. Microemulsion formulation and plain drug solution were placed in the donor compartment of two separate diffusion cells and the temperature of each cell was maintained at 37 ±2°C. The amount of drug released from the microemulsionformulation can be estimated spectrophotometrically at specific wavelength, by withdrawing samples from the receptor compartment at predetermined time intervals.

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J.APPLICATIONS OF MICROEMULSIONS

There has been a revolution in the last two decades in the utilization of microemulsion systems in a variety of pharmaceutical, chemical, industrialMicroemulsions.

1. Microemulsion in pharmaceutical

Liquid crystalline, miceller and emulsion forming systems are widely used in pharmaceutical preparations. The easy formation, remarkable environment independent stability, excellent solubilization capacity, etc. favour microemulsions to be a better proposition over other compartmentalized systems. The dispersed phase, lipophilic or hydrophilic(o/w or w/o type) can act as a potential reservoir of lipophilic or hydrophilic drugs that can be partitioned between the dispersed and the continuous phases. Coming in contact with a semipermeable membrane, such as skin or mucous membrane, the drug can be transported through the barrier. Both lipophilic and hydrophilic drugs can be administered together in the same preparation.

Low viscous formulations using microemulsions with suitable protein compatible surfactants can be used as injection solutions, for they are miscible with blood in any ratio. In contrast to emulsions, microemulsions cause minimum immuno reactions or fat embolism. Proteins are not denatured in microemulsions although they are unstable at high or low temperatures. The total dose of the drug can be reduced when applied through the microemulsion route and thus side effects can be minimized.

Toxicity, bio-incompatibility of surfactants and cosurfactants, requirement of high concentrations for formulations and other relevant factors such as maintenance of thermodynamic stability in the temperature range between 0 ^{0}C and 40 ^{0} C, salinity, constant pressure during storage, low solubilizing capacity for high molecular weight drug (and oil), etc. limit the uses of microemulsions in the pharmaceutical and medicinal fields.

An application of o/w microemulsion in the pharmaceutical industry is the use of strongly hydrophobic fluorocarbons (as oils) to produce short-time blood plasma substitutes to maintain the supply of oxygen in the living systems. The components to be used must have low allergic potential, good physiological compatibility and high biocompatibility. The biocompatibility requirements of the amphiphiles are fulfilled by lecithins, non-ionic surfactants (Brijs, Arlacel 186, Spans and Tweens).

Garcia-Celma has reviewed microemulsions as drug delivery systems for different types of drugs, viz. antineoplastics/ antitumour agents (doxorubicin, idarubicin, tetrabenzamidine derivative), peptide drugs (cyclosporine, insulin, vassopressin), sympatholytics (bupranolol, timolol, levobunolol, propanolol), local anesthetics (lidocaine, benzocaine, tetracaine, heptacaine), steroids (testosterone, testosterone propionate, testosterone enanthate, progesterone, medroxyprogestorane acetate), anxiolytics(benzodiazepines), antiinfective drugs (cloitrimazole, ciclopiroxolamine, econazole nitrate, tetracycline hydrochloride), vitamins (menadione, ascorbic acid), anti-inflammatory drugs(butibufen, indomethacin), and dermological products(tyrocine, azelaic acid, octyl dimethyl PABA, 2- ethyl hexyl *p*-methoxycinnamate).

Enzyme doped silica nanoparticles (ceramic drug carrier) in the aqueous core of reverse micelles and microencapsulation of diospyrin, a plant-derived bisnapthoquinol of potential chemotherupic activity have been very recently reported.

2. Microemulsions in cosmetics:

It is believed that microemulsion formulation will result in a faster uptake into the skin. Cost, safety, appropriate selection of ingredients are key factors in the formulation of microemulsions. Skin care microemulsions contain , sodium alkyl sulfate, tetraethylene glycol monododecyl ether, lecithin, dodecyl oligoglucoside, alkyl dimethyl amine oxide, propanol,hexadecane, isopropyl myristate have been used as surfactants, cosurfactants and oils respectively. Hair care microemulsions contain an amino-functional polyorganosiloxane (a nonionic surfactant) and an acid and/or a metal salt.

Cosmetic microemulsions (transparent and translucent) of silicone oils was produced by emulsion polymerization tehnique. Ultrafine 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. Tokuoka*et al.*studied the solubilization of several systems consisting of water, surfactant and synthetic perfumes (viz. d-limonene, *a*-ionone, benzyl accetate, linalol, eugenol and *a*-hexylcinnamaldehyde), clarifying (a) the influence of fragrance structure on the phase regions in a water/nonionic surfactant systems, (b) the distribution

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coefficient between micelles and the bulk phase, and (c) the partition between dissolved and solubilized perfume components on their volatility. In this, the phase equilibria in water, lecithin, soybean oil and vanillin have been studied.

3. Microemulsions in analytical applications:

Microemulsions are widely used in the field of analytical techniques such as chromatography, laser-excited photoionization spectroscopy, etc. In microemulsionelectrokinetic chromatography (MEEKC), characterization of solute hydrophobicity was carried out , which provides a quick and reproducible method to obtain hydrophobic parameters for solvents. Microemulsions are able to enhance analytical spectroscopic techniques by functioning as solubilized media, spectral shift reagents, intensity amplification agents, etc. The utilization of microemulsion media in analytical spectroscopy and the analytical sensitivities of the three systems o/w, w/o and bicontinuousmicroemulsion have been assessed. A series of studies have been reported on the determination of aluminium, zinc, copper, cadmium, manganese ions using both microemulsion and mixed microemulsion systems. These studies are mostly published in the journals published by the Chinese Chemical Society.

4. Microemulsions in biotechnology:

Recently, interest on microemulsions is being focused for various applications in biotechnology, viz, enzymatic reactions, immobilization of proteins and bioseparation. Microemulsions are advantageous over other multiphase equilibrium systems because of simultaneous solubilization of polar and nonpolar reactants in the same solution, shifting of the equilibrium position of the reaction and the separation of products by physical means. However, bio-incompatibility of the amphiphiles used poses a serious limitation in the advancement of this field. The prospects of biotechnological applications have also been reviewed. Enzyme reactions (catalysis) in microemulsion media have widely been studied. The use of microemulsion for enzyme catalysis is not arbitrary for enzymes under *in vivo* condition function in the cell as well as at the interface of hydrophobic and hydrophilic domains of cell and tissue containing lipids and other natural amphiphiles.

5. Enzymatic reactions in microemulsions:

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 microemulsion 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. The conformation and activity of an enzyme depend on ([water]/[surfactant]); the enzyme is thus sensitive to amount of surrounding water.
Gomez-Puyon has carried the work on behaviour of enzymes in microemulsions

Immobilization of protein in microemulsion: In the field of protein immobilization, microemulsion medium has been found to be a good proposition. Immobilization of a variety of proteins on suitable solid surfaces using microemulsion media has been successfully carried out

Microemulsions for bioseparations*:* The possibility of microemulsions to extract biopolymers (proteins and enzymes) from an aqueous phase has been explored. Microemulsions are gentle solvents for extraction of proteins without altering their enzymatic or functional properties although the process can readily be scaled by conventional liquid–liquid extraction techniques. The pH, ionic strength, type of salt, concentration of solvent and temperature
influence the partition of a protein.

6. **Microemulsion as chemical sensor materials.**

Microemulsions as novel crystalline colloidal arrays (CCA) are new findings which acts as novel chemical sensors. A intelligent photoionic crystalline colloidal array self assemblies have been developed, which can have use in medicine, environmental chemistry, process control and remote sensing. These are mesoscopically periodic fluid materials, that diffract light satisfying the Bragg condition.
The crystalline colloidal array self assemble into either face centered or body centered cubic form. Just as atomic crystals diffract X-rays that fulfill the Bragg condition, CCAs diffract ultraviolet, visible and near-infrared light, depending on the lattice spacing. Colloidal particles of inorganic materials, such as silica or organic polymers, such as

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poly (*N*isopropylacrylamide) have been synthesized having periodicity of the order of ~200 nm. Asher *et al.* and Holtz *et al.* have developed a novel sensing material from a polymerized crystalline colloidal array (PCCA) which is a mesoscopically periodic crystalline colloidal array of spherical polystyrene colloids within a thin, intelligent polymer hydrogel film. They have fabricated a sensor, utilizing a crown ether as the recognization agent that can detect Pb2+ in the 0.1 M– 20 mM (~20 ppb – ~ 400 ppm) concentration range. The sensors for glucose and galactose utilising glucose oxidase or *b*-D-galactosidase as the recognization entities have been developed. Besides sensing glucose, this sensor can estimate dissolved oxygen concentration in the presence of constant glucose concentration. Development of thermally tunable photonic crystal of poly (*N*-isopropylacrylamide) (PNIPAM), a novel CCA photoionic crystals with variable sphere sizes and variable array periodicity and sensors that change volume in response to nonionic molecular recognition processes such as antibody/antigen interactions have been attempted.

II.CONCLUSION

Microemulsions are having a vast and significant potential in drug delivery as well as in the industrial process. Researchers are working in this field for drug release, coatings, dyes, agrochemicals and in enzyme reaction. In the future prospects, microemulsions will be used in synthesis of nanoparticles and as a industrial chemical sensors. The role of microemulsion in providing novel solutions to overcome the problems of poor aqueous solubility of highly lipophilic drug compounds and provide high, more consistent and reproducible bioavailability. Furthermore, these formulations can be easily manufactured in term of the relative cost of commercial production. Topical products are now employing the microemulsion technology are likely to emerge. Microemulsions can also be used to achieve drug targeting however challenges remain, primarily because of the layers of barriers that these systems need to overcome to reach to the target. Recent research work is focused on the production of safe, efficient and more compatible microemulsion constituents which will further enhance the utility of these novel vehicles. Microemulsion in today's world can be accepted as full of potential in a novel drug delivery systems.

REFERENCES

1. Cortesi R and Nastruzzi C. Liposomes, micelles and microemulsions as new delivery systems for cytotoxic alkaloids. *PSTT* 1999; 2: 288-98.
2 baße A and Keipert S. Development and characterization of microemulsions for ocularapplication. *Europ. J. Pharm. Biopharm*1997; 43: 179-83
3 Paul BK, Moulik SP. Microemulsions: an overview. J DisperSciTechnol 1997;18: 301 -306.
4 Prince LM. Microemulsions. In: Lissant KJ (ed). Emulsions and Emulsion Technology. New York : Marcel Dekker; 1974. 125-178.
5 Delgado-Charro MB, Iglesias-Vilas G, Blanco-Mendez J, Lopez- Quintela MA, Marty JP, Guy RH. Delivery of a hydrophilic solute through the skin from novel microemulsion systems. Eur J Pharm Biopharm 1997; 43: 37-42.
6 Celebi N, Kıslal O, Tarımcı N. The effect of βcyclodextrin and penetration additives on the release of naproxen from ointment bases. Pharmazie 1993; 48: 914-917.
7 Gupta P, Vermani K, Garg S. Hydrogels from controlled release to pH-responsive drug delivery. Drug Discov Today 2002; 7: 569-579.
8 Turner SR, Siano DB and J. Bock,A. Microemulsion Process for Producing Acrylamide-Alkyl Acrylamide Copolymers, U. S. Patent No. 4,521,580, June 1985.
9 Gasco M R, Gallarate M, Trotta M, Bauchiero L, Gremmo E, Chiapperomicroemulsion review. J. Pharm. Biomed. Anal 1989; 7: 433-440
10 Siebenbrodt I., KeipertS microemulsion a review.: Eur. J. Pharm. Biopharm 1993; 25-32.
11 Ghosh PK, Majithiya RK, Umrethia ML, and Murthy RSR. Design and Development of Microemulsion Drug Delivery System of Acyclovir for Improvement of Oral Bioavailability. AAPS PharmSciTech 2006; 7 (3),77-82.
12 Eccleston, J. Microemulsions, in: J. Swarbrick, J.C. Boylan (Eds.), Encyclopedia of Pharmaceutical Technology, Vol. 9, Marcel Dekker, New York, 1994, 375–421.
13 Lawrence, M.J. Surfactant systems: microemulsions and vesicles as vehicles for drug delivery, Eur. J. Drug Metab. Pharmacokinet. 1994; 3: 257-269.
14 Lawrence, M.J. Micro emulsions as drug delivery vehicles, Curr. Opin. Colloid Interface Sci. 1996; 1: 826–832.
15 Eccleston GM, Swarbick J, Boylan JC. Emulsion and Microemulsions in Encyclopedia of Pharmaceutical Technology. 2002; 2(5),1080-1085.
16 Bagwe RP, Kanicky JR, Palla BJ, Patanjali PK, and Shah D. Center for surface science and engineering, Dept. of chemical engineering, university of Florida, Gainesville, fl 32611. Improved drug delivery using microemulsions. 2001; 18 (1): 123-126
17 Jadhav KR, Shaikh IM, Ambade KW, Kadam VJ. Applications of microemulsion based drug delivery system.2006; 267-73.
18 Bidyut KP, Satya PM. Uses and applications of microemulsions. Current Sci. 2001; 80 (8): 990-1001.
19 Gupta,raviReview on occular drug delivery;Ijpr2001;16(2):125-129.
20 Singhkhushboo, Sharma monica, Ram gopal college of pharmacy, Gurgaon Recent trends and future prospects self emulsifying drug delivery system;1-9, Reference Id: PHARMATUTOR-ART-1174.
21 Grampurohit N, Ravikumar P and Mallya R. Microemulsions for Topical Use. Ind J of Pharm Edu. 2011; 45(1):100-107.
22 Park KM and Kim CK. Preparation and evaluation of flurbiprofen-loaded microemulsions for parental delivery. Int J Pharm. 1999; 181: 173-179.