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Preparation of Microemulsion for Transedermal Drug Delivery System

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Abstract: ***The microemulsion is a very suitable carrier medium for the drug delivery system. With the help of microemulsion penetrate the suitable drug in the body by oral, topical, and parenteral administration. The microemulsion is thermodynamically stable isotropically clear dispersion of two immiscible liquid, such as oil and water and stabilized by an interfacial film of surfactant and co-surfactant molecules. Currently the microemulsion is a rising worldwide importance in a variety of technological application. Microemulsion behave like supersolvents of drug. There are advantages that they can solubilize both hydrophilic and hydrophobic drug. In this review brief discussion about microemulsion such as definition, types, formation characteristics, stability, the effect of additives, pressure, temperature on the phase behavior of microemulsion.***

Keywords: Microemulsion, Stability, Surfactant, Transdermal delivery

1. Introduction

Microemulsion is the very suitable topical carrier medium system in which the drug are easily delivered across the skin. They are thermodynamically stable transparent, isotropic and colloidal. It is the dispersed system having oil phase and water phase and combination of surfactant and co-surfactant. Globules diameter is less than 100 nm (10-100) in form of liquid solution.[13,7] The viscosity of the microemulsion electrolyte is increased when the concentration of viscous alcohol is increased, causing a reduction in the EOF velocity. The droplet also increases in size as it incorporates more co-surfactant, reducing both its charge density and its electrophoretic mobility. In this one liquid are dispersed in another liquid. The mechanism are micelle formation of the concentration of liquid immersed surfactant are make the medium of oil and aqueous phase head of the surfactant that is hydrophilic are attached to the water molecules and lipophilic tails are attached to the oil droplets. Microemulsion systems are also called in other form such as transparent emulsion, swollen micelle, micellar solution, and solubilised oil.

2. Structure of Microemulsion

Micro emulsions or Micellar emulsion are dynamic system in which the interface is continuously and spontaneously fluctuating.7Structurally, they are divided in to oil in water (o/w), water in oil (w/o) and bi-continuous micro emulsions. In w/o micro emulsions, water droplets are dispersed in the continuous oil phase while o/w micro emulsions are formed when oil droplets are dispersed in the continuous aqueous phase. In system where the amounts of water and oil are similar [5], the bi-continuous micro emulsions may result.8The mixture oil water and surfactants are able to form a wide variety of structure and phase depending upon the proportions of component [1].

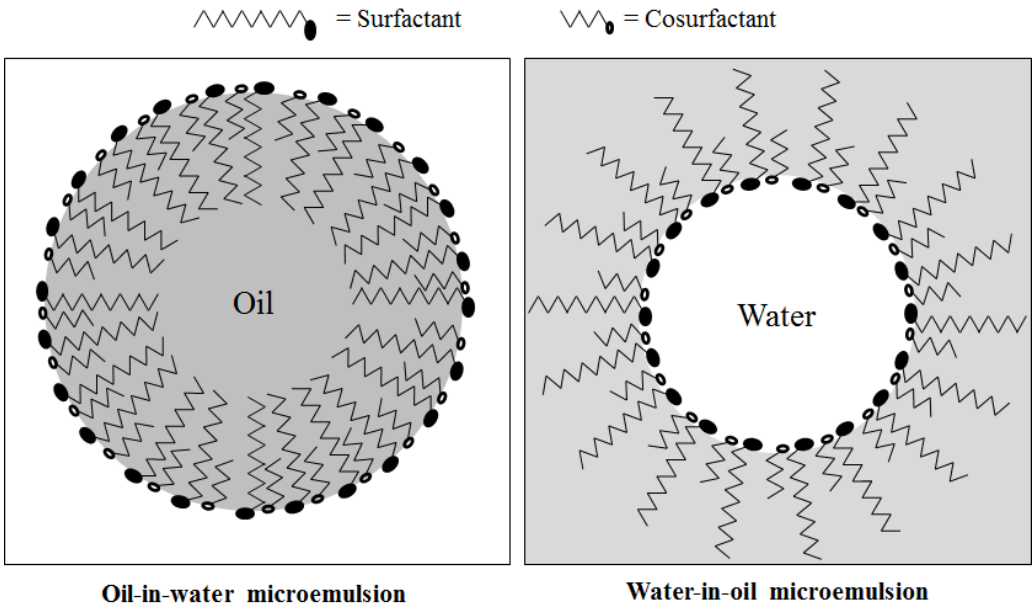
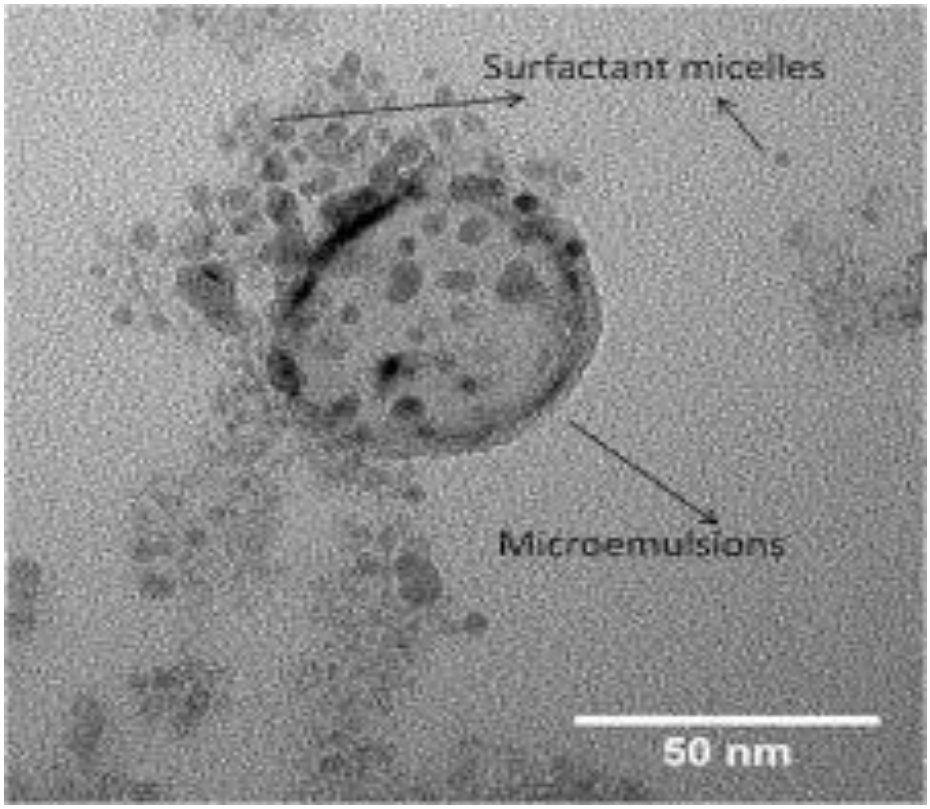


Figure: Microemulsion



Visual image of Microemulsion

Types of Microemulsion

Microemulsion are thermodynamically stable. The microemulsion are form by the combination of oil, water, surfactant and usually co-surfactan[4]. That is ane droplet or continuous phase there is three types of microemulsion[3].

1) Oil-In-Water Microemulsion
2) Water-In-Oil Microemulsion
3) Bicontinuous Microemulsion

Oil-In-Water Microemulsion

Oil in water types microemulsion are droplet of oil surrounded by a surfactant (and if co-surfactant) film form the internal phase distributed in the water and water in continuous phase[1]. This type of microemulsion generally has a larger interaction volume than the w/o microemulsions. The monolayer of surfactant forms the interfacial film that is oriented in a "positive" curve, where the polar head-groups face the continuous water phase and the lipophilic tails face into the oil droplets. [7]

Water-In-Oil Microemulsion

Water-in-oil microemulsions are made up of droplets of water surrounded by an oil continuous phase. These are generally known as "reverse-micelles", where the polar headgroups of the surfactant are facing into the droplets of water, with the fatty acid tails facing into the oil phase. A w/o microemulsion used orally or parenterally may be destabilized by the aqueous biological system. The biological system increases the phase volume of the internal phase, eventually leading to a "percolation phenomenon" where phase separation or phase inversion occurs

Bicontinuous Microemulsion

When the amount of water and oil present are similar [4]. Continuous microemulsion system may result. In this case, both water and oil exist as a continuous phase. Irregular channels of oil and water are intertwined, resulting in what looks like a "sponge-phase". Transitions from o/w to w/o microemulsions may pass through this bicontinuous state. Bicontinuous microemulsion, may show non-Newtonian flow and plasticity[1,2] These properties make them especially useful for topical delivery of drugs or for intravenous administration, where upon dilution with aqueous biological fluids, form an o/w microemulsion [11].

Composition of Microemulsion

The Major component in micro emulsion system are[18]-

1) Oil phase
2) Surfactant (primary surfactant)
3) Co-surfactant (secondary surfactant)
4) Co-solvent

Component	Example
Oil	1-saturated fatty acid-lauric acid, carpic acid 2-unsaturated fatty acid-oleic acid, linolic acid, linolenic acid 3-fatty acid ester-ethyl or methyl ester of lauric, oleic acid and myristic acid
Surfactant	1-polyoxyethylene/polysorbate/tween 20, 40, 60, 80 2-sorbitan monolaurate,eggs lecithin 3-sodium dodecyl sulphate
Co-surfactant	1-ethanol, proranol, butanol, isopropanol, pentanol, hexanol 2-polyoxyethylene-10-oelyl ether 3-sodium monohexyl phosphate 4-cinnamic alcohol,cinamic alcohol
Aqueous	1-water

Methods of Preparation of Microemulsion

Microemulsion are formed only when Interfacial tension at the oil/water interface is brought to very low level Interfacial layer is kept highly flexible and fluid Concentration of surfactant must be high enough to provide the number of surfactant molecules needed to stabilize the microdroplets to be produced by an ultra low interfacial tension There are mainly two methods by which we can formulate microemulsion, which are as follows[12] Titration Method A mixture of fatty acid and oil is added to a caustic solution to produce a microemulsion, which is then titrated with a cosurfactant, an alcohol, until the system turned clear. It is found that as the chain length of the surfactant increased, microemulsions with significant transmittances by visible spectrum can be formed with oils of longer chain lengths. It is also found that different alcohols affect the formation of microemulsions in different ways[11] The amount of surfactant and cosurfactant to be added and the percent of oilphase that can be incorporated shall be determined with the help of pseudo-ternary phase diagram. Ultrasonicator can finally be used so to achieve the desired size range for dispersed globules [13] .

Theories of Microemulsion [19]

Various theories concerning microemulsion formation, stability and phase behavior have been proposed Thermodynamic Theory [2, 7]

Microemulsion formation and stability can be explained on the basis of simplified thermodynamic rationalization. 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 the change in entropy of the system such that[20],

DG f = γDA - T DS

where DG f = Free Energy of formation,

γ =Surface Tension of the oil–water interface,

DA = Change in interfacial area on microemulsification,

DS = Change in entropy of the system which is effectively the dispersion entropy, and

T = Temperature.

It should be noted that when a microemulsion is formed the change in DA is very large due to the large number of very small droplets formed The dominant favourable entropic contribution is the very large dispersion entropy arising from the mixing of one phase in the other in the form of large numbers of small droplets. However, favourable entropic contributions also arise from other dynamic processes such as surfactant diffusion in the interfacial layer and monomer-micelle surfactant exchange [15] microemulsification is spontaneous and the resulting dispersion is thermodynamically stable.

Characteristics

These new systems are “micro emulsions”. The interfacial tension between phases, amount of energy required for formation, droplet sizes, and visual appearance are only a few of the differences seen when comparing emulsions to micro emulsions. Water-in-oil micro emulsionsare also known as reverse micelles[6] These systems have the ability to solubilise both hydrophilic and hydrophobic substances. Micro emulsions usually exhibit low viscosities and Newtonian flow characteristics. Their flow remains constant when subjected toa variety of shear rates. Discontinuous formulations may show some non-Newtonian flow and plasticity. Micro emulsion viscosity is close to that of water[17], even at high droplet concentrations. The microstructure constantly changes, making them very dynamic systems with reversible droplet coalescence. A variety of techniques are employed to characterize different properties of micro emulsion [1,4,9].

Factor affecting Microemulsion

Factor affecting the micro-emulsion given in bellow;

- Packing ratio
- Property of surfactant
- Property of oil phase
- Temperature
- Chain length
- Nature of co-surfactan

Application of Microemulsion

The application of micro-emulsion is given in the bellow

- Ophthalmic delivery system
- microemulsion in detergency
- microemulsion in cosmetics
- microemulsion in food
- Oral delivery system
- Parental delivery system

Conclusion

Microemulsion isdrug delivery systems for the delivery of more than one medicament simultaneously his article focuses on types of microemulsion, composition of microemulsion, preparation & evaluation of microemulsion, While microemulsions are used in several fields[6,7], this article focuses on the reported investigations for different applications 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.The drug delivery through the microemulsion is a promising area for the continued research with the aim of achieving the controlled release with enhanced bioavailability and for drug targeting to various sites of the body [8, 9].

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