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Microemulsion

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ABSTRACT:-

Improving the bioavailability of drugs is one of the biggest challenges in drug formulation. Among various approaches, microemulsion, which is a clear, stable, isotropic mixture of oil, water, and surfactant, has gained more attention due to increased oral bioavailability, protection of labile drug, control of drug release, enhancement of drug solubility, and reduction of patient variability. This review concerns the fundamental work characterizing the physicochemical behavior of microemulsions that needs to be done before they can live up to their potential as multipurpose drug carriers. In order to appreciate the potential of microemulsions as delivery vehicles, this review provides an overview of the formation, phase behavior, characterization of microemulsions and their application in various drug delivery routes.

KEYWORDS:- microemulsion, phase behavior, drug delivery, Solubilization.

INTRODUCTION:-

The term microemulsion, also called transparent emulsion, swollen micelle, micellar solution, and solubilized oil, was first used by Jack H. Shulman in 19591. Microemulsions are defined as thermodynamically stable, transparent (translucent) dispersions of oils and water that are stabilized by an interfacial film of molecules surfactants. The surfactant may be pure, mixed, or combined with a cosurfactant such as a medium chain alcohol (eg, butanol, pentanol). These homogeneous systems, which can be prepared in a wide range of surfactant concentrations and oil-to-water ratios (20-80%), are all low-viscosity liquids. Microemulsions are easily distinguished from normal emulsions by their transparency, low viscosity and above all by their thermodynamic stability and ability to spontaneously form2.

Microemulsion systems consisting of at least 30% oil, 1 to 30% nonionic surfactant system with a hydrophilic lipophilic balance, HLB, containing between 9 and 18, 20% cosolvent and at least 30% water can form spontaneously and are therefore thermodynamically stable. For this reason, microemulsion systems have a theoretically infinite shelf life under normal conditions in contrast to the limited shelf life of macroemulsions. Furthermore, the droplet size in such microemulsions remains constant and ranges from 100-1000 A0 (10-100 nm) and has a very low oil/water interfacial tension. Because the droplet size is less than 25% of the wavelength of visible light, microemulsions are transparent3,4.

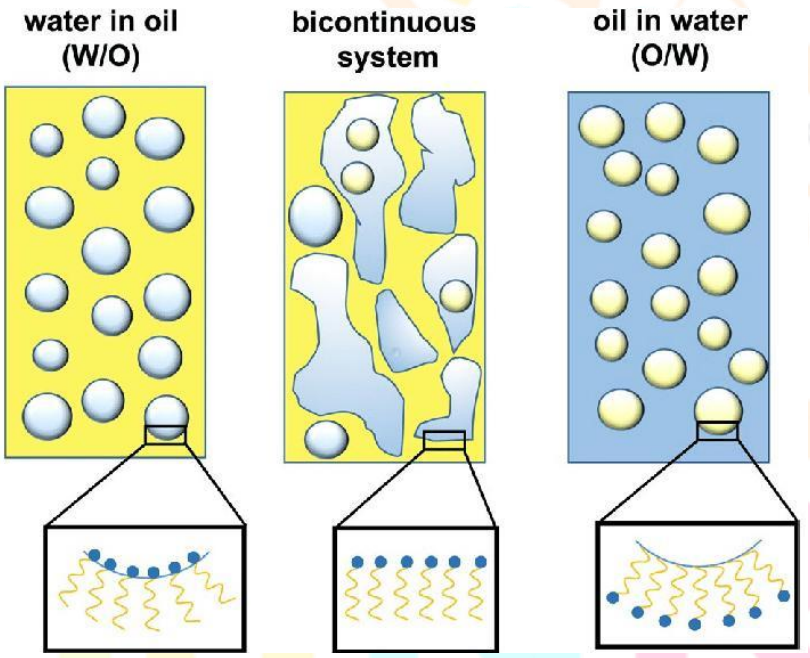
Three distinct microemulsion solubilization systems that can be used for pharmaceuticals are as follows:

1. Oil in water.

2. Water in oil.

3. Bi-continuous microemulsion.

In all three types of microemulsions, the is stabilized by a suitable combination of surfactants



Advantages of Microemulsion Based Systems:[7]

Microemulsions are a thermodynamically stable system, and the stability enables self-emulsification of the system.

· The property of microemulsions does not depend on the process used.

· They can solubilize both hydrophilic and lipophilic drugs, including drugs that are relatively insoluble in both aqueous and hydrophobic solvents. That is why they are called supersolvents. This property of microemulsions is due to the formation of microdomains of different polarity in the same single-phase system.

· The hydrophilic or lipophilic dispersed phase can act as a reservoir for lipophilic or hydrophilic drugs.

· Drug release through the membrane follows pseudo-zero-order kinetics and depends on the volume of the dispersed phase, the distribution of the drug, and the rate of drug transport across the membrane.

· Microemulsions can be sterilized by filtration due to their small size.

· The same microemulsion can carry both a lipophilic and a hydrophilic drug.

· Microemulsions are easy to prepare and do not require any significant energy input during preparation.

· Microemulsions improve the effectiveness of the drug and make it possible to reduce the total dose.

Disadvantages of Microemulsion Based Systems:[7]

. A high concentration of surfactant and co-surfactant is required.

· Limited solubilizing capacity for substances with a high melting point.

· The surfactant must be non-toxic for use in pharmaceutical applications.

· Microemulsion stability is affected by environmental parameters such as temperature and pH. These parameters change after delivery of the microemulsion to patients.

Method 11 of Preparing a Microemulsion:

A method of forming a microemulsion includes the following steps: Forming a mixture of liquids to produce a microemulsion-forming liquid system.

. To divide the liquid mixture into at least two mixture streams.

. Pressurize each fluid stream to a minimum of 4000 psi.

. Discharge each pressurized streamthrough a suitable nozzle at a velocity of at least 40 m/s into a low pressure zone filled with mixture.
Mixed flows converge in this low pressure zone.
These create a turbulent jet interaction of the flow along a common boundary.

• The microemulsion has a diameter ofabout 1 μm or less and comprises droplets of the dispersed phase forremoving the formed microemulsion from the low pressure zone.

Solubilization of Poorly Soluble Drugs 3:
Solutions, Emulsions, Microemulsions,and Micelles

The interactions between solutes and solvents can be qualitatively andquantitatively modified to improve drug solubility. For example, using buffers to adjust pH to increase ionization of weakly acidic or weakly basic drugs enhances the ionic dipole interaction between solute and solvent. The addition of co-solvents lowers the dielectric constant of water and promotes hydrophobic interactions between drug molecules and the solvent system.

Mechanisms of Solubility Enhancement

In the presence of significant amounts of oil, surfactants concentrate at the oil/water interface and form:
· If the oil content is low, small surfactant beads encased in oil form, so-called swelling micelles or microemulsions.
· The active ingredient can be solubilized in the oily core and/or at the interfaces of these structures. The major site of drug solubilization depends on its hydrophobicity and interaction with surfactants and/or cosurfactants.
· Microemulsions differ from emulsions by the amount of dispersed phase, unlikemicelles in the presence of oil.

· Microemulsions often require co-solventsand/or co-surfactants to facilitate their formation. Both microemulsions and micelles are suitablefor preparing aqueous solutions of hydrophobic drugs.
· The physical properties, drug entrapment mechanisms, andphysicochemical interactions of theconstituents of these systems determinedrug dissolution capacity and physical stability during storage and dilution.

Drug entrapment and structure:

· The location of solubilized drugs in microemulsion systems depends on the hydrophobicity and structure of the solute. The maximum amount of hydrophobic drug solubilized depends on the curvature of the interface.
· The interfacial surfactant layer exhibitsa positive curvature towards the dispersed phase. This is determined by both the relative volume of the dispersed phase and the spontaneous curvature of thesurfactant molecules. The drug loading capacity is higher when the drug molecule uptake is facilitated at the interface and the natural curvature is smaller than the actual curvature.
· Using phase equilibrium analysis, theinterfacial partition coefficient of solutes was weakly dependent on surfactant concentration rather than on solute concentration and aggregate shape. highly depends on factors affecting the surface pressure or the bending moment of the surface film. B. Solvent type and external electrolyte type and concentration.
· The presence of the solute itself affects the system depending on the propertiesof the solute and surfactant. The phenomenon of drug solubilization at the interface affects not only drug loading capacity but also drug precipitation upon dilution.

Microemulsion solubilization capacity:

microemulsion systems can often solubilize larger amounts of drug than theindividual components. This high solubilization capacity was attributed to the interfacial sites for drug solubilization, which have a higher solubilization capacity than the core. Higher interfacialsolubilization capacity is a function of drug-surfactant interactions leading to drug association at the interface. These interactions depend on the hydrophobicity, functional groups, and morphology of the drug and surfactant/co-surfactant. The solubilization capacity decreasesprogressively with water dilution when the micellar system reaches the o/w microemulsion system via the swollen w/o reverse micelles of the bicontinuous phase. Evaluation of drug solubilizingcapacity at various dilution levels allows formulators to define an appropriate dilution range for a given formulation with minimal potential for drug precipitation.

Microemulsion solubilization capacity:

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Microemulsion Characterization:

Includes physical and chemical testing associated with oral liquid dosage forms. Relates to composition effects on physical parameters such as assay, content uniformity, active substance (impurity) stability, appearance, pH, viscosity, density, conductivity, surface tension, dispersed phase size and zeta potential do.

Microemulsion Applications in Formulations:

Solid Controlled Release Microemulsion:

Microemulsion is used to form a controlled release product by dispersing themicroemulsion in a vehicle and mixing until uniform. The solvent is then removed by methods such as evaporation under reduced pressure, spray drying, etc., resulting in solidification and controlled release of the drug from the microemulsion21.

Nanocapsules from W/O microemulsions:

The advantage of producing PECA nanocapsules by interfacial polymerization of water-in-oil microemulsions over other methods is that they maintain stability and can be used with certain bioactive substances, especially proteins. It may be related to achieving efficient encapsulation of peptides. Various physicochemical properties of nanocapsules such as size, wall thickness, polymer molecular weight, and release rate can be controlled by manipulating some of the formulation variables. B. Amount of monomer used, water weight fraction of aqueous component of microemulsion,and pH 22. Anju Graf et al. also mentioninsulin nanoparticles prepared from w/o microemulsions by interfacial polymerization method 23 .

Nanosuspension:

Michele Trotta et al. describes the formulation of griseofulvin nanoparticles from water-dilutable microemulsions. Using optimized formulations, thisnanosuspension can be prepared by microemulsion diffusion techniquesusing pharmaceutically acceptable solvents such as butyl lactate. Sub-100 nm griseofvin nanoparticles with low polydispersity were obtained. The dissolution rate of griseofulvin particles obtained by the solvent diffusion method was higher than that of commercial products24.

Drug Delivery Applications:

Parenteral Use:

microemulsions are used for parenteraldrug delivery due to their small particle size and low viscosity. Chong-Kook Kim et. Al. Phospholipid-based microemulsions were prepared using ethanol as a co-solvent by the natural emulsification method. Plasma concentrations of flurbiprofen after intravenous microemulsion administration were similar to concentrations after commercial liposuction. However, the T1/2, AUC and MRT of the flurbiprofen-loaded microemulsion were significantly increased. This microemulsion may also reduce uptake into RES-rich organs due to the increased surface hydrophilicity of the microemulsion, which is one of the properties of this particular drug delivery system 25 . Chong-Kook Kim et. Al. We are also investigating a parenteralformulation of ATRA. This formulation overcomes that solubility limitation by using a phospholipid-based microemulsion system as a carrier26. Jiang Ping Jewett. Al. We have studied the use of chitosan in microemulsion formulations. Chitosan may significantly increase the brain uptake of nobiletin while decreasing the concentration of drug delivered to the heart and kidneys.

Transdermal Application:

transdermal formulations have the advantage over oral formulations as first-pass metabolism, thus increasing bioavailability. Ljiljana Djordjevic and al. studied microemulsionsfor the delivery of amphiphilic drugs for skin application, drug effects on vehicle microstructure, and drug release kinetics. Jane Lawrence and others formulated gelatin-stabilized microemulsion-based organogels and also studied their rheology and applications in iontophoretic transdermal drug delivery. Urti et al. Estradiol microemulsion formulated for topical administration. Microemulsion formulations increased estradiol flux 200- to 700-fold over controls, but decreasedpermeability coefficients by 5- to 18-fold.The superior transdermal flux of estradiol was due to a 1500-fold improvement in solubilization of estradiol

by microemulsion. This result suggests that microemulsions are a potential vehicle for enhancing topical delivery of estradiol.

Oral **Formulations:**

microemulsion formulations have superior bioavailability compared to other oral formulations such as hydroalcoholic solutions, suspensions and coarse emulsions. Sylvie Crust-Mancier et al. described improved oral bioavailability of cefpodoxime proxetil by formulating asubmicron oil-in-water emulsion31. Kosaku Kawakami and others. We worked on a microemulsion formulation known to improve the bioavailability of poorly soluble drugs. Nitrendipine has been used as a sparingly soluble model drug and its absorption was significantly improved using a microemulsion formulationcompared to suspensions or oil solutions32. Chong-Kook Kim et al.described the improved bioavailability of cyclosporin A by using an O/Wmicroemulsion. This enhancement is believed to be due to a combination of factors, including drug solubilizing effects and increased drug permeability across the intestinal membrane. In other words, the bioavailability of drugs loaded into microemulsions depended on the physicochemical properties of the drug and the o/w microemulsion33. Stretched

SMEDDS:

SMEDDS contains the **n**on-aqueous component of the microemulsion and when diluted with an aqueous phase with gentle stirring readily disperses to form a microemulsion. SMEDDS are often preferred over microemulsion formulations of hydrolysis-sensitive drugs, and their small volume allows them to be packaged in soft gelatin capsules for oral administration. A self-microemulsifyingdrug delivery system (SMEDDS) to improve the oral bioavailability of thepoorly water-soluble drug simvastatinwas studied by Sun Hang Choc et al. Hiroshi Aratani formulated a new O/W Hismicroemulsion formulation that improvesoral bioavailability by increasing the solubility of poorly water-solublecompounds. The solubility-improvingeffect of this O/W microemulsion has been studied for about 11 poorly water-soluble compounds such as ibuprofen, ketoprofen, chloramphenicol, testosterone, tolbutamide, tamoxifen, disopyramide, and other new compounds. increase.

Others:

Ljiljana Djordjevic et. We investigated the effects of both formulation parameters and carrier structure on the in vitro release kinetics of the amphiphilic drug diclofenac diethylamine (DDA) from microemulsions51. Trotta et al. al. studied the phase behavior of a microemulsion system containing lecithin and lysolecithin as surfactants52. Ruth Shett. al. He studied the phase behavior and particle size analysis of oil-in-water phospholipid microemulsions53.

Conclusions:

microemulsion is a system that uses large amounts of surfactants to solubilize drugs. Therefore, for lipophilic drugs, it can also increase drug solubility. Dosage forms such as microemulsions offer useful solutions to stability and bioavailability issues. Microemulsions prepared using oils, surfactants and co-surfactants were stable and clear for anacceptable period of time. It is also a very useful drug delivery technique when rapid access to drugs is required.

Microemulsions protect labile drugs, control drug release, increase drug solubility, increase bioavailability, and reduce patient variability, as well as formulate formulations suitable for most routes of administration. is shown. However, there is still a considerable amount of fundamental work to characterize the physicochemical behavior of microemulsions that needs to be performed before realizing their potential as versatile drug delivery vehicles.

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