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MICROEMULSION: Novel drug delivery system for delivery of drug

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Abstract:

Microemulsions, which are optically isotropic and thermodynamically stable system capacity to solubilize poorly, water soluble drugs as well as their enhancement of topical availability. The hydrophilic and lipophillic both can deliver easily from microemulsion, the microemulsion have quality to improve solubilization of drug, maintain drug's shelf life,it is also beneficial for improve bioavailability. The microemulsion Provides protection from hydrolysis and oxidation as drug in oil phase in O/W microemulsion is not exposed to attack by water and air. The term microemulsion is also describing a variety of physical system, including swollen micelles O/W and W/O microemulsion, bicontinous structure. It is promising for both transdermal and dermal delivery of drug as an efficient route of administration. The microemulsion with its compound is easily able to reduce the diffusional barrier of the stratnum corneum and increase the permeation of drug.

Keywords: - Micro-emulsion, topical drug delivery, Pseudo-ternary phase diagram, surfactants, lipophilic drug.

1. Introduction

Microemulsion system is better known as the composition of oil phase, aqueous phase, surfactant and cosurfactant at appropriate ratio. The size consist of microemulsion is 10-100nm. It has specific property like transparency, optical isotropy, low viscosity and thermodynamic stability. It follows the three mechanism-first, the high solubility potential for lipophilic and hydrophilic drug of the microemulsion system might increase thermodynamic activity, Second ingredients of the system act as permeation enhancer. Third the drug to the internal phase could be modified easily so the drug can be increased due to affinity of drug to internal phase. The "microemulsion" refers as a thermodynamically stable, The two immiscible liquid like oil and water got in their isotropic dispersion, which can be easily stable by surfactant by reduce the interfacial tension. Surfactant molecules contain both a polar as well as an apolar group. So they exhibit a very peculiar behavior, they get adsorbed at the interface in begining, where they can fulfill their dual affinity with hydrophilic groups located in aqueous phase and hydrophobic groups in oil or air. After that, they reduce mismatching with solvent by Micellization Process. The dispersed phase cosidered of small particles or droplets,generally the microemulsion will be transparent because of the wavelength of visible

light which have very small droplet size,less than 25%. The microemulsion is formed readily and sometimes spontaneously, generally without high-energy input.

1.1 Advantages of microemulsion:

Microemulsions system has considerable potential to act as a drug delivery vehicle by Incorporating a wide range of drug molecules.

- It is promoting as a vehicle for topical, oral, nasal and transdermal applications.
- It is helpful for bioavailability enhancers for poorly water soluble drug.
- A large amount of drug can be integrate in the formulation due to high solubilizing capacity that might increase the thermodynamic activity towards the skin.
- The permeation rate of the drug from microemulsion may be increased, since the affinity of a drug to the internal phase in micro emulsion can be easily modified to favorportioning into stratum corneum, using different internal phase, changing its portion in microemulsion.
- The percutaneous delivery of the drug will also increase due to hydration effect of stratum corneum by absorption, if the water content in microemulsion is high enough.

1.2 Importance of microemulsions:

- The rate of absorption is increased.
- Eliminates variability in absorption.
- Helps to solublize lipophilic drug.
- An aqueous dosage form will be available easily espacially for water insoluble drugs .
- Increases bioavailability of drug.
- Various routes like tropical, oral and intravenous can be used as medical device to deliver the product.
- Helpful to provide better taste masking
- Liquid dosage form increases patient compliance.

2. Phase rule: The phase rule enables identification of the number of variables depending on system compositions and conditions. It is depicted as

$F = C - P + 2$

Where, F is the number of possible independent changes of state or degrees of freedom, C the number of independent chemical constituents and P the number of phases present in system. The F value determines the system to be invariant, monovariant, bivariant etc depending on its value whether zero, 1, 2 or so on. At low surfactant concentration, there is series of

equilibria between phases, referred as winsor phases

Winsor I: The microemulsion phase (o/w) is in equilibrium with the upper excess oil. The surfactant rich water phase coexists with oil phase where surfactant is only present as monomers at small concentration.

Winsor II: The upper microemulsion phase (w/o) is in equilibrium with excess of water. The surfactant rich oil phase coexists with surfactant poor aqueous phase.

Winsor III: The middle microemulsion phase (o/w plus w/o called bicontinuous) is in equilibrium with excess oil and lower excess water. Surfactant rich middle phase coexists with both excess water and oil surfactant poor phase

Winsor IV: Here oil, water and surfactant are homogenously are mixed to form isotropic single phase micellar solution.

Inter-conversion between these phases can be produced by adjusting the proportions of components. Phase transitions are brought by increasing either electrolyte concentration in case of ionic surfactants or increasing temperature in case of non ionic surfactants15. Various investigators have explored on interactions in adsorbed interfacial film to explain the direction and extent of curvature. R-Ratio was first proposed by Winsor to account for influence of amphiphiles and solvents on interfacial curvature. The R- ratio compares tendency for amphiphile to disperse in oil, to its tendency to dissolve in water. The R- ratio of cohesive energies coming from interaction of interfacial layer with oil, divided by energies resulting from interactions of water determines the preferred interfacial curvature. A balanced interfacial layer is represented by R=1.

3. Components of Microemulsion:

- **Oil phase** - The selection of oil is based on the nature of the drug as well as the route of administration. The screened oil should have solubilisation potential for the drug. Saturated and unsaturated fatty acids have penetration enhancing activity of their own. Recent trend is towards use of semisynthetic oils that are more stable than their natural counterparts. Poorly aqueous soluble drugs need to have solubility in dispersed oil phase to form efficient o/w microemulsion system. Even with increase in oil content in o/w microemulsions leads to increase in droplet size
- **Surfactant-** Surfactants are the molecules which when present in low concentration will adsorb to the surface of interfaces of a system and alter the interfacial energies of the system. The actual purpose of surfactant is to lower the interfacial tension to negligible value that facilitates the process of dispersion

during preparation of microemulsion. Surfactant screening can be done with help of HLB (Hydrophilic lipophilic balance) value. The HLB provides a numerical value that suggests whether o/w or w/o emulsion will form. It relates molecular structure to interfacial packing and film curvature

- **Cosurfactant-** In most of the cases, single chain surfactants alone are incapable to reduce o/w interfacial tension sufficiently to form microemulsion. Owing to its amphiphilic nature, a co-surfactant accumulates substantially at interfacial layer, increasing the fluidity of interfacial film by penetrating into surfactant layer.
- **Aqueous phase-** Water is most commonly used as aqueous phase. in case of microemulsions used for parenteral administration aqueous phase should be isoosmotic to blood which is adjusted by sodium chloride, glycerol, dextrose and sorbitol. The pH of aqueous phase always needs to be adjusted due to its considerable impact on phase behavior of microemulsions

4. Method of preparation:

- Phase titration method
- Phase inversion method

4.1 **Phase titration method**: Microemulsions are constructing by spontaneous emulsification method which is obtained by help of phase diagrams. Different componants and its mixer is helpful to construction of phase diagram which is helpful to study of complex series of microemulsion.pseudo-ternary phase diagrams are constructed to figure out microemulsion zone,with the study got that as quaternary phase diagram consume the time more and its difficult to interpret.

4.2 **Phase inversion**: Phase inversion promotes to radical physical changes that alters drug release. 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 with suitable surfactant to spontaneous formation.

5. Characterization of microemulsion:

The morphology of microemulsion can be study by using electron microscopy. The average droplet diameter of microemulsion determined by photon correlation spectroscopy instrument. The viscosity of microemulsion should be measured by suitable viscometer. The conductivity and pH is also important parameter. Centrifugation is helpful to determine the stability of microemulsion. Invitro and invivo is also important and mandatory parameter for stable microemulsion.

5.1 Droplet size measures-Size analysis of microemulsion can be investigated by electron microscopy. Size analysis can also studied out by dynamic light scattering experiments. It is most important technique because it directly produces images at high resolution and it can capture any co-existent structure and microstructural transitions. It is

also known as Transmission Electron Microscopy (TEM) method.

5.2 Zeta potential measurements-It is confirmatory test to known the nature of microemulsion. Zeta potential for microemulsion was observed by using zetasizer Dilution test method to know about the tendency of ME.98

5.3 Viscosity measurement- The viscosity of microemulsions of several compositions can be measured at different shear rates at different temperatures using Brookfield type rotary viscometer. The instrument sample room should be maintained at temparature 37 ± 0.2°C.

5.4 In vitro drug permeation studies- Franz diffusion cells with a cellulose membrane are utilized to determine the Release rate of drug from different microemulsion formulations.The cellulose membrane is first hydrated in the distilled water solution at 25 0C for 24 hours. The membrane is then clamped between the donor and receptor compartments of the cells Diffusion cell was filled with 25 ml of phosphate buffer (pH = 7.4) and methanol (1:2). The magnetic bar will be helpful to stirrer vigorously at 600 RPM.The Microemulsion will be accurately weight and placed in donor compartment. At 0.5, 1, 2, 3, 4, 5, 6, 7, 8 and 24 h time intervals, 2 ml sample is removed from receptor for spectrophotometric determination and replaced immediately with an equal volume of fresh receptor solution. Samples are analyzed using UV visible spectrophotometer. The result will be obtained in plotted form between drug percent v/s time

5.5 Stability studies-The physical stability of the microemulsion must be determined under different storage conditions (4, 25 and 40 °C). Fresh preparations as well as those that have been kept under various stress conditions for extended period of time were subjected to droplet size distribution analysis.

6. Conclusion-

Today microemulsions have been shown interested in many matter control drug release, increase drug solubility, increase bioavailability, reduce patient variability increase the rate of absorption, helps solublize lipophilic drug, various routes like tropical, oral and intravenous can be used to deliver the product, helpful in taste masking, provides and increases patient compliance. Moreover, the nature of microemulsions was found to be a crucial parameter for permeation of an active ingredient. The microemulsion formulations are helpful for the delivery of hydrophilic and lipophilic drug both are as drug carriers due to their improved drug solubilisation capacity, and forlong shelf life, ease of preparation and improvement of bioavailability.

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