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Microemulsion: A review

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ABSTRACT

Microemulsions are one of the most important novel drug delivery systems because of their long shelf life, improved drug solubilization with ease of preparation and administration. This emulsion is thermodynamically stable and optically isotropic liquid solutions of oil, water, and amphiphile. Microemulsions well as novel vehicles for drug delivery that allow controlled or sustained release for ocular, percutaneous, topical, transdermal, and parenteral administration of medicaments. Distinguish is very easy from microemulsion to normal emulsions by their low viscosity, transparency, and more accurately their thermodynamic stability. It Application has a great range and uses such as in pharmaceuticals, agrochemicals, cutting oils, biotechnology, food, cosmetics, analytical applications, environmental detoxification, etc. The purpose of this review paper is to discuss microemulsions as drug carrier systems with other possible applications.

Key words: Microemulsions, thermodynamically stable, amphiphile, solubilization

INTRODUCTION

Microemulsion is a dispersion of droplets of one liquid in another immiscible liquid. The droplets are termed the dispersed phase, while the second liquid is the continuous phase. Microemulsion is divided in two types:water□in□oil (w/o) and oil□in□water (o/w). As the name signal, water is the dispersed phase in w/o emulsions, whereas oil is the dispersed phase in o/w emulsions[1]. The most important different between macro emulsions and microemulsions is that the size of the droplets of the dispersed phase of microemulsions is between 5 and 100 nm, while that of macroemulsions is>100 nm. Microemulsions are thermodynamically and kinetically stable systems[2]. Microemulsions are translucent and of low viscosity, while macroemulsions are opaque and of relatively high viscosity. Due to these unique properties of microemulsions, these systems have become indispensable in numerous important fields. The droplets in a microemulsion are in the range of 0.1-1.0μm [3]. Microemulsion shows miscellaneous structural organization due to the use of wide range of surfactant concentration, water-oil ratios, temperature etc. In case of

emulsion, it contains three components, namely oil, water and surfactant; whereas microemulsions generally require a fourth component *i.e.,*cosurfactants, which include linear alcohols of medium chain length that is miscible with water. The surfactant and co-surfactant combined promotes the generation of extensive interfaces through the spontaneous dispersion of oil in water, or vice-versa. Large interfacial area between oil and water consists of a mixed interfacial film containing both surfactant and co-surfactant molecules. Interfacial tension of oil-water interfaces in emulsions approaches zero, which also contributes to their spontaneous formation. Microemulsions are regarded as micelles extensively swollen by large amounts of solubilized oil[4-12].

ADVANTAGES OF MICROEMULSION SYSTEM[13-18]

1. Microemulsions can easily prepared and require no energy contribution during preparation this is due to better thermodynamic stability.
2. Microemulsions are thermodynamically stable system and allow self-emulsification of the system.
3. Microemulsions have low viscosity compared to emulsions.
4. Microemulsions act as super solvents for drug, can solubilise both hydrophilic and lipophilic drugs including drugs that are insoluble in both aqueous and hydrophobic solvents.
5. Microemulsion having the ability to carry both lipophilic and hydrophilic drugs.
6. The dispersed phase, lipophilic or hydrophilic(O/W, or W/O microemulsions) can act as a potential reservoir of lipophilic or hydrophilic drugs, respectively.
7. Microemulsion used as delivery systems can improve the efficacy of a drug, allowing the total dose to be reduced and thus minimizing side effects.

DISADVANTAGES OF MICROEMULSION SYSTEMS[19-21]

1. Microemulsion having limited solubilizing capacity for high melting substances.

2. Require large number of Surfactants for stabilizing droplets.

3. Microemulsion stability depends on the temperature and pH.

TYPES OF MICROEMULSIONS[22-25]

1. Oil-in-water microemulsion
2. Water -in-oil microemulsion
3. Bi-continuous microemulsion
4. Single phase homogeneous mixture

OIL- IN- WATER MICROEMULSION

This type of microemulsions droplets of oil is surrounded by a surfactant (and maybe co surfactant) film that forms the internal phase distributed in water, which is the continuous phase. Oil in water generally has a larger interaction volume than the w/o microemulsions.

WATER - IN - OIL MICROEMULSION

In this type of microemulsions droplets of water surrounded by a continuous oil phase. Microemulsion are recognized as "reverse micelles", where the polar head groups of the surfactant are facing into the droplets of water, with the fatty acid tails facing into the oil phase. Generally, water in oil microemulsion used orally or parenterally may be destabilized by the aqueous biological system.

BI-CONTINUOUS MICROEMULSION

In this system the amount of water and oil present are similar, in this case, both water and oil exist as a continuous phase. Transitions from o/w to w/o microemulsions may pass through this bi-continuous state. Bi-continuous microemulsion, may show non-Newtonian flow and plasticity.

METHOD OF FORMULATION[26-36]

Two type of method of preparation are reported for microemulsion,

1. Phase Inversion Method
2. Phase Titration Method

PHASE INVERSION METHOD

In this method phase inversion of microemulsions occurs by addition of excess amount of the dispersed phase. For the non-ionic surfactants, this

can be completed by changing the temperature, forcing a transition from oil in water microemulsion at low temperatures to water in oil microemulsion at higher temperatures(transitional phase inversion). Until the cooling, the system crosses a point of zero spontaneous curvature and minimal surface tension, promoting the formation of finely dispersed oil droplets. This technique is also known as phase inversion temperature method. Beyond, a transition in the spontaneous radius of curvature can be obtained by changing the water volume fraction. When increasing the water volume fraction changes the spontaneous curvature of the surfactant from initially stabilizing a w/o microemulsion to an o/w microemulsion at the inversion point.

PHASE TITRATION METHOD

Microemulsions are prepared by the spontaneous emulsification method (phase titration method) and can be shown with the help of phase diagrams. The mixture of fatty acid and oil is added to a caustic solution to prepare a microemulsion, then after it is titrated with a co surfactant, an alcohol, until the system turned clear. Phase titration method in 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 also found that different alcohol affects the formation of microemulsions in different ways.

EVALUATION PARAMETERS OF MICROEMULSION SYSTEM[37-51]

VISUAL INSPECTION

By the visual inspection, we can check the properties such as fluidity, homogeneity, and optical clarity.

PERCENT TRANSMITTANCE TEST (LIMPIDITY TEST)

The Percent Transmittance Test of the microemulsion can be measured spectrophoto metrically using a spectrophotometer.

MEASUREMENTS OF DROPLET SIZE

Size examination of micro-emulsion can be obtained by Dynamic-Light-Scattering experiments or electron microscopy. The polydispersity can be done by a similar Instrument.

ZETA-POTENTIAL DIMENSIONS AND GLOBULE-SIZE

Zeta-Potential and Globule-Size of the micro-emulsion can be resolute by Dynamic-Light-Scattering, via a ZETASIZERHAS-3000.

EXAMINATION UNDER CROSS-POLARIZING MICROSCOPE

The nonappearance of fringe on the way to eliminate Liquid- Crystalline-Systems, the micro-emulsion must be examined under a cross polarizing microscope.

DRUG STABILITY

The microemulsion optimized was kept under cold conditions (4-8°C), room temperature, and at elevated temperature (50 ± 2 °C). Every 2 months the microemulsion can be analyzed for phase separation, % transmittance, globule size, and % assay.

ASSESSMENT OF THE RHEOLOGICAL PROPERTIES (VISCOSITY MEASUREMENT)

The rheological properties play an important role in instability. It can be determined by Brookfield's digital viscometer. Change in the rheological characteristics helps in determining the microemulsion region and its separation from another region. Bi-continuous microemulsions are dynamic structures with continuous fluctuations occurring between the bi-continuous structure, swollen reverse micelle, and swollen micelles.

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 at ambient temperature and at a constant frequency of 1 Hz.

DRUG SOLUBILITY

Drug 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 the drug in microemulsion was compared with respect to its individual ingredients.

IN-VITRO DRUG RELEASE

In vitro, a drug release diffusion study can be carried out on a modified Franz diffusion cell, within the volume of 20mL. The receptor compartment was filled with 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 a specific wavelength.

APPLICATION OF MICROEMULSION[51-58]

ORAL ADMINISTRATION

Oral administration of micro emulsion formulations offers several benefits over conventional oral formulation including increased absorption, improved clinical potency, and decreased drug toxicity. Therefore, micro emulsion has been reported to be an ideal delivery of drugs such as steroids, hormones, diuretic and antibiotics. However, most are difficult to administer orally. With on oral bioavailability in conventional (i.e., non-micro emulsion based) formulation of less than 10%, they are usually not therapeutically active by oral administration.

PARENTERAL DELIVERY

This administration of drugs with limited solubility is a major problem in industry because of the extremely low amount of drug actually delivery to a targeted site. This type 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.

TOPICAL DELIVERY

This type administration of drugs can have advantages over other methods for several reasons, one of which is the avoidance of hepatic first-pass metabolism, salivary and degradation of the drug in stomach and related toxicity effects. They are able to incorporate both hydrophilic (5-fluorouracil, apomorphine hydrochloride etc) and lipophilic drugs (oestradiol, finasteride, ketoprofen etc) and enhance their permeation. This type of emulsion formation requires high surfactant concentration, the skin irritation aspect must be considered especially when they are intended to be applied for a longer period.

OCULAR AND PULMONARY DELIVERY

This delivery is used for the treatment of eye diseases, drugs are essentially delivered topically. Oil-in-water microemulsions have been investigated for ocular administration, to dissolve poorly soluble drugs, to increase absorption and to attain prolong release profile.

MICROEMULSIONS IN BIOTECHNOLOGY

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

1. Increased solubility in non-polar reactants.

2. The Possibility of shifting thermodynamic equilibria in favour of condensations.

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

MICRO EMULSIONS IN COSMETICS

Cosmetic applications such as skin care products, emulsions are widely used with water as the

continuous phase. Cost, safety (as many surfactants are irritating to the skin when used in high concentrations), appropriate selection of ingredients (*i.e.,* surfactants, co surfactants, oils) are key factors in the formulation of micro emulsions[34].

LUBRICANTS, CUTTING OILS AND CORROSION INHIBITORS

Micro emulsions or reverse micellar solutions are in use as lubricants, cutting oils and corrosion inhibitors for several decades. The presence of surfactant in micro emulsion 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 micro emulsion cannot react with the metal surface and on the other, the metal surface is protected by the adsorbed hydrophobic surfactant film. In micro emulsions, water with much higher thermal conductivity, imparts higher heat capacity to the system.

MICROEMULSIONS IN ANALYTICAL APPLICATIONS

This emulsions widely used in the field of analytical techniques such as chromatography etc. In microemulsion electro kinetic chromatography (MEEKC), characterization of solute hydrophobicity was carried out, which provides a quick and reproducible method to obtain hydrophobic parameters for solvents. The utilization of microemulsion media in analytical spectroscopy and the analytical sensitivities of the Microemulsions have a really crucial importance within the drug delivery system also as within the process. They can be wont to optimize drug targeting without a concomitant increase in systemic absorption. Microemulsions also can be wont to achieve drug targeting however challenges remain, primarily due to the layers of barriers that these systems got to overcome to succeed in to the target. Furthermore, it's proven possible to three systems o/w, w/o and bi continuous microemulsion have been assessed.

MICROEMULSIONS IN ENHANCED OIL RECOVERY

Mechanisms of enhanced oil recovery (EOR) using surfactant and microemulsion can help in obtaining unrecoverable underground oil. If the interfacial tension between the crude oil and reservoir brine can be reduced to around 10-3 mN/m, a substantial fraction of the residual oil in the porous media in which it is trapped can be mobilized. Low interfacial viscosity of the system is also advantageous.

- Microemulsions for bio separations
- Microemulsion as a chemical sensor material
- Microemulsions as lubricants, cutting oils and corrosion inhibitors
- Microemulsions as coatings and textile Finishing
- Microemulsions in detergency.
- Microemulsions in cosmetics.
- Microemulsions in agrochemicals.
- Microemulsions in food.
- Microemulsions in environmental remediation and detoxification.
- Micro porous media synthesis (microemulsion gel technique).
- Microemulsions in analytical applications.
- Microemulsions as liquid membranes.
- Novel crystalline colloidal arrays as chemical sensor materials.

CONCLUSION

formulate preparations suitable for many routes of administration. In today's world Microemulsion is accepted as filled with potential for novel drug delivery systems. Current research work is concentrated on the preparation of safe, efficient and more compatible microemulsion constituents which can further enhance the utility of those novel vehicles.

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