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Microemulsions for Topical Drug Carrier: A Review

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Abstract
Recent days microemulsion is a novel drug carrier system of oil, water and a surfactant with a co-surfactant. Microemulsions are monophasic, thermodynamically stable species with much smaller droplet diameter (20 to 200 nm) and thus are visually transparent or translucent and having ultra low interfacial tension. Microemulsion has low viscosity with Newtonian behaviour and is highly flexible. Microemulsion can be classified as oil-in-water (o/w), water-in-oil (w/o) or bicontinuous system depending on their structure. Microemulsion is easy to prepare and does not require maximum energy of formation. In the present study, we discuss about the various advantages of microemulsion in pharmaceuticals, along with the preparation, evaluation and research work carried out on microemulsions.
Key words: microemulsion, advantages of microemulsion, material and methods, topical delivery

Introduction

Our exclusive reliance on traditional routes of drug administration is being currently challenged by the aggressive imaginative thinkers in the pharmaceutical and biotechnological industries. Innovative research targeted at novel sites for administration(mucous membranes, skin) and elimination of discomfort associated with drug administration will ultimately affect critical care practice beyond the now common practice of skin patches (piddle, 1992). Microemulsions are clear, thermodynamically stable, isotropic liquid mixtures of oil, water and surfactant, frequently in combination with a cosurfactant. The aqueous phase may contain salt(s) and/or other ingredients, and the "oil" may actually be a complex mixture of different hydrocarbons and olefins. 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 three basic types of microemulsions are direct (oil dispersed in water, o/w), reversed (water dispersed in oil, w/o) and bicontinuous.

Successful topical delivery of drugs has always remained a challenge to the drug delivery field, since approximately 40% of the new drug candidates have poor water solubility, and thus topical delivery is frequently associated with implications of low bioavailability. Microemulsions have attracted considerable amount of interest as potential drug delivery vehicles, largely due to their simplicity of preparation, clarity and ability to be filtered and incorporate a wide range of drugs of varying solubility. Oil-in-water (o/w) microemulsion is the most suitable formulation, which is expected to increase the solubility by dissolving compounds with low water solubility into an oil phase. They can also enhance bioavailability by reducing the droplet size (20-200 nm), and hence increase the rate of absorption due to surfactant-induced permeability changes.

Type of Microemulsion:

(a) o/w microemulsion
(b) w/o microemulsion

Advantages of Microemulsion system:

1. They provide excellent thermodynamic stability.
2. They act as super solvents, improving the solubility and thermodynamic activity of the drug.
3. The small particle size of the microemulsion as well as both the hydrophilic and lipophilic domains of microemulsion enhances the percutaneous uptake of the drugs.
4. They act as potential reservoir of the drugs, through which pseudo-zero order kinetics can be obtained.

5. The small size of the droplets provides large interfacial area from where drug can be quickly release, improving the oral absorption of poorly water soluble drugs.
6. They are easy to prepare with no significant energy contribution.
7. They can improve the efficacy of the drug allowing the dose reduction side effect minimization.
8. They prevent hydrolysis and oxidation of the drug when the drug is in oil phase *(Vyas and Khar 2002).*

Disadvantages of Microemulsion:

1. In many cases high concentration of surfactant and co-surfactants is required to formulate a stable microemulsion.
2. A relatively small number of pharmaceutically acceptable excepients are available to be used in microemulsion formulation.

Material and Methods of Microemulsion Formulation

Material

Oil Phase

Lipophilic drugs are preferably solubilised in o/w microemulsions. The main criterion for selecting the oil phase is that the drug should have high solubility in it.[(1)] The oil component also influences curvature by its ability to penetrate and hence swell the tail group region of the surfactant monolayer.[(2)] Short chains oils penetrate the lipophilic group region to a great extent and result in increased negative curvature.

Surfactants

The type of microemulsion depends on the nature of surfactant. Surfactant contains hydrophilic head group and lipophilic tail group. Generally non-ionic surfactants are chosen because of their good cutaneous tolerance, lower irritation potential and toxicity.[(10,29,30)]

The areas of head and tail group, 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.

Co-surfactants

In most cases, single-chain surfactants alone are unable to reduce the 0/w interfacial tension sufficiently to enable a microemulsion to form.[(3-6)] The presence of co-surfactants allows the interfacial film sufficient flexibility to take up different curvatures required to form microemulsion over a wide range of composition.[(7-9)]

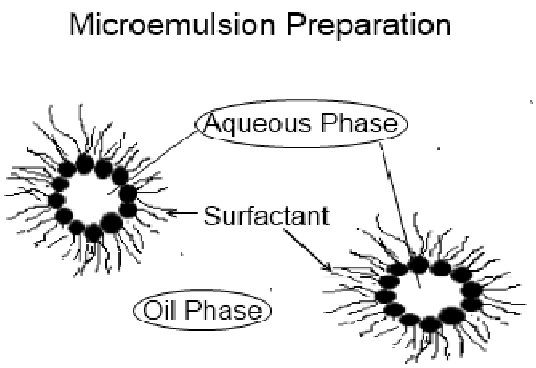

Fig.1: Different phase of Microemulsion

Method of Preparation

Microemulsions are thermodynamically stable, so they can prepare simply by blending oil, water, surfactant and cosurfactant with mild agitation or mild heat. There are two methods of preparation of microemulsion.

1. Phase Titration Method

Microemulsions are prepared by the spontaneous emulsification method also known as phase titration method and can be depicted with the help of phase diagram. Construction of phase diagram is a useful approach to study the complex series of interaction of different components. Pseudo ternary phase diagram is often consist different zones, in which each corner of the diagram represent 100% of the particular component.[(11,12)]

2. Phase Inversion Method

Phase inversion of microemulsions occurs upon addition of excess of the dispersed phase or in response to temperature. In this method physical changes occur including changes in particle size that can affect drug release both in vivo and in vitro. These methods make use of changing the spontaneous curvature of the surfactant.[(1,12)]

Factor Affecting the Microemulsion

1. Packing ratio

The HLB of surfactant determine the type of microemulsion through its influence on molecular film and packing curvature.

Critical packing ratio is given by:

$$c.p.p = V / (a \times l)$$

Where **V** is volume of surfactant, **a** is head group surface area and **l** is length.
If c.p.p is between 0-1, interface curves towards water (positive), if c.p.p is greater than 1, interface curves towards oil (negative) and if c.p.p is equal to 1, then either bicontinuous or lamellar structure. [2, 13]

1. Property of surfactant, oil phase and temperature

The most important criterion for screening f components is the solubility of poorly soluble drug in different oils, surfactant and cosurfactant. The type of microemulsion depends on the nature of surfactant because it contains hydrophilic head group and lipophilic tail group. The oil component influences curvature by its ability to penetrate and hence swell the tail group region of the surfactant monolayer.

Generally used oils and surfactants are:

Oil: oleic acid, ethyl oleate, mineral oil, isopropyl myristate, decanol, vegetable oil like as coconut oil, Safflower oil, soyabean oil, olive oil etc.

Surfactant: Lecithin, polyglyceryl1-6-dioleate, Polysorbate (Tween 80, Tween 60 and Tween 20) etc.

2. The chain length, type and nature of cosurfactant

Different types of alcohol are widely used as a cosurfactant in microemulsion formulation. It is also affect the curvature of the microemulsion.

Commonly used co surfactants are: Isopropyl alcohol, capryol 90, ethanol, monostearate, propylene glycol.

Evaluation of Microemulsion

Phase behaviour studies

Visual observation, phase contrast microscopy and freeze fracture transmission electron microscopy can be used to differentiate microemulsions from liquid crystals and coarse emulsion. 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.

Rheology

Change in the rheological characteristics help in determining the microemulsion region and its separation from other related structure like liquid crystals. Bicontinuous microemulsions are dynamic structures with continuous fluctuations.

Scattering Techniques

Scattering techniques such as small angle neutron scattering, small angle X-ray scattering and light scattering have found application in studies of microemulsion structure, especially in case of dilute monodisperese spheres.

Microemulsion in Topical Drug Delivery

Microemulsions are promising delivery systems[26-27]that allow sustained or controlled drug release for percutaneous, topical, ocular, peroral, transdermal and parenteral administration. A topical treatment of several diseases is often limited by the poor percutaneous permeation through the human skin. For this reason the realization of topical formulations with are able to improve the percutaneous permeation of antifungal drugs can be of particular importance for the success of topical therapeutic approaches. The common method to improve drug permeation through the skin is to use permeation enhancers i.e. organic solvent and fatty acids. Penetration enhancers can change the structure of the skin lipids and alter the skin barrier function. The compounds, even if they increase the transdermal flux of several drugs often generate skin irritation. Other methods have been proposed to increase the permeability of drugs through the skin i.e. iontophoresis and ultrasound, but these methods are frequently not used due to the requirement of qualified staff for their application. Recently some methods have proposed the use of substance endowed with low toxicity, i.e. phospholipids as penetration enhancers. These substances present a notable affinity with cellular membranes thus leading to an increased absorption of several drugs. Various lipid based topical formulations have been proposed as dermal and transdermal drug delivery system i.e. liposomes and microemulsions. Microemulsions present some advantages like storage stability, formulation ease and better drug loading that make them potential system useful for the delivery of drug candidates across the skin. There various type of topical delivery based microemulsion like as antifungal, antiviral, anti acne, antioxidants, ocular, spermicidal and cosmetics.

Result and Discussion

Microemulsions are thermodynamically stable and isotropic liquid solution of oil, water and surfactant with a cosurfactant. They are now being widely investigated for preparing personal care products. There is growing recognition of the potential benefits of microemulsions in the field of cosmetics and other topical dosage forms in addition to drug delivery. They can be used to optimise drug targeting without a concomitant increase in systemic absorption.

Conclusion

Microemulsions are thermodynamically stable, transparent, low viscosity mixtures of oil and water stabilized by a monolayer of surfactant. The chemistry of microemulsions is at an incredibly exciting stage of development. The

advent of systems that are easy to handle allows those without specialist knowledge of the field to use them for the first time. Because of its versatility and thermodynamic stability, the microemulsion systems find potential applications in pharmaceutical, oil recovery, as food additives and as reaction media, etc. There are different theories which have been developed over the course of time relating to the formation of microemulsions.

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