Academic Sciences

International Journal of Current Pharmaceutical Research

ISSN- 0975-7066 Vol 5, Issue 2, 2013

Review Article

A REVIEW ON MICROEMULSIONS

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Received: 29 January 2013 , Revised and Accepted: 02 March 2013

ABSTRACT

Microemulsions have emerged as novel vehicles for drug delivery which allow sustained or controlled release for percutaneous, peroral, topical, transdermal, ocular and parenteral administration of medicaments. They offer the advantage of spontaneous formation, ease of manufacturing and scale-up, thermodynamic stability, improved drug solubilization of hydrophobic drugs and bioavailability.

Keywords: Microemulsions, Topical delivery, Surfactants, Cosurfactants.

INTRODUCTION

Microemulsions have been widely studied to enhance the bioavailability of the poorly soluble drugs. They offer a cost effective approach in such cases. Microemulsions have very low surface tension and small droplet size which results in high absorption and permeation. Interest in these versatile carriers is increasing and their applications have been diversified to various administration routes in addition to the conventional oral route. This can be attributed to their unique solubilization properties and thermodynamic stability which has drawn attention for their use as novel vehicles for drug delivery. The results obtained have been indeed very promising. In recent past, microemulsion formulation of a poorly soluble immunosuppressant was marketed as a soft capsule which contains a mixture of drug dissolved in oil and surfactant [5-7]. It converts into an oil-in-water (o/w) microemulsion *in situ* in an aqueous environment in the stomach and the small intestine. Microemulsion formulation made the bioavailability and plasma concentration profiles of the drug more reproducible which is clinically important in the case of drugs showing serious adverse effects. This is a significant step forward in the delivery of poorly soluble drugs. Microemulsion systems are also now being increasingly investigated for transdermal [8], ocular [10], nasal [11], pulmonary, vaginal [12], rectal and intravenous drug delivery.

Microemulsions have advantages over both colloidal systems under investigation and conventional emulsions, suspensions and micellar solutions and may provide alternative drug **:** carriers . They are promising delivery systems which allow sustained or controlled drug release for percutaneous, peroral, topical, transdermal, ocular and parenteral administration of medicaments. They offer the advantage of spontaneous formation, ease of manufacturing and scale-up, thermodynamic stability, improved drug solubilization of hydrophobic drugs and bioavailability. Also microemulsions that have inverse micellar structure may be less comedogenic than either creams or solutions.

Hoar and Schulman defined as a transparent solution obtained by titrating a normal coarse emulsion with medium-chain alcohols. Microemulsions are thermodynamically stable isotropic systems in which two immiscible liquids (water and oil) are mixed to form a single phase by means of an appropriate surfactant or its mixture. The short to medium chain alcohols are generally considered as co-surfactants in the microemulsion system. The presence of surfactant and cosurfactant in the system makes the interfacial tension very low. Therefore microemulsions form spontaneously, with an average droplet diameter of 10 to 140 nm.

Microemulsions have the ability to deliver larger amounts of water and topically applied agents into the skin than water alone or other traditional vehicles such as lotions or creams because they act as a better reservoir for a poorly soluble drug through their capacity for enhanced solubilization. The main difference between macroemulsions and microemulsions lies in the size and shape of the particles dispersed in the continuous phase: these are at least an order of magnitude smaller in the case of microemulsions (10-200 nm) than those of conventional emulsions (1-20 m). Macroemulsions consist of roughly spherical droplets of one phase dispersed into the other whereas microemulsions constantly evolve between various structures ranging from droplet-like swollen micelles to bicontinuous structures, making the usual “oil in water” and “water in oil” distinction sometimes irrelevant.

APPLICATIONS OF MICROEMULSIONS

Microemulsions are promising delivery systems that allow sustained or controlled drug release for percutaneous, peroral, topical, transdermal, ocular and parenteral administration. Enhanced absorption of drugs, modulation of the kinetics of the drug release and decreased toxicity are several advantages in the delivery process. The following is a compilation of reported literature for topical microemulsions. Antifungal agents eg miconazole, ketoconazole, anditraconazole being lipophilic in nature have been formulated as microemulsions to impart to them the advantages like ease of preparation due to spontaneous formation, thermodynamic stability, transparent and elegant appearance, increased drug loading, enhanced penetration through the biological membranes, increased bioavailability compared to [7, 8] conventional dosage forms. .

Anti acne

Novel drug delivery strategies like microemulsions can play a pivotal role in improving the topical delivery of antiacne agents by enhancing their dermal localization with a concomitant reduction in their side effects Microemulsions of azelaic acid, a bioactive molecule used in many skin disorders, prepared using the monosodium salt (AZA-Na) have been evaluated as delivery vehicles.

Antiviral

A study was done to investigate and evaluate microemulsion and microemulsion-based hydrogel as a topical delivery system for penciclovir in comparison with a commercial cream. The results of permeation test *in vivo* in mice showed that as compared with the commercial cream, microemulsionbased hydrogel and microemulsion could significantly increase the permeation of penciclovir into both epidermis and dermis. Stability tests showed that microemulsion-based hydrogel stored at 4 °C for 3 months had no significant change in physicochemical properties. Skin irritation test in rabbits demonstrated that single application or multiple applications of microemulsion-based hydrogel did not cause any erythema or edema.

Antioxidants

Antioxidants have been used in dermatological and cosmetic products because of their property of scavenging and destroying aggressive oxidizing agents and free radicals that are involved in various skin conditions.

Ocular

Eye drops account for 90% of the available ophthalmic formulations due to their simplicity and convenience. However, rapid precorneal loss caused by drainage and high tear fluid turnover is amongst the major problems associated with topical ophthalmic drug delivery. microemulsions provided a promising alternative with improved ocular retention, increased corneal drug absorption and reduced systemic side effects whilst maintaining the simplicity and convenience of the dosage form as eye drops.

Spermicidal

O.D'Cruz described a formulation of novel gelmicroemulsions (GM) as nontoxic, dual-function intravaginal spermicides, which could be used as delivery vehicles for lipophilic drug substances targeting sexually transmitted pathogens. These GMs comprising oil-in-water microemulsion and polymeric hydrogels were designed to solubilize lipophilic antiviral/antimicrobial agents.

Cosmetics

There is growing recognition of the potential benefits of microemulsions in the field of cosmetics in addition to drug delivery. They are now being widely investigated for preparing personal care products with superior features such as having improved product efficiency, stability, appearance and minimal irritation. Microemulsions are also suitable in perfumery so as to minimize the quantity of organic solvents

Structure

Microemulsions are dynamic systems in which the interface is continuously and spontaneously fluctuating. Structurally, they are divided into oil-in-water (o/w), waterin- oil (w/o) and bicontinuous microemulsions. In w/o microemulsion, water droplets are dispersed in the continuous oil phase while o/w microemulsion is formed when oil droplets are dispersed in the continuous aqueous phase. In systems where the amounts of water and oil are similar, a bicontinuous microemulsion may result. In all three types of microemulsions, the interface is stabilized by an appropriate combination of surfactants and/or co-surfactants. The mixture of oil, water and surfactants is able to form a wide variety of structures and phases depending upon the proportions of the components. The flexibility of the surfactant film is an important factor in this regard. A flexible surfactant film will enable the existence of several different structures like droplet like shapes, aggregates and bicontinuous structures, and therefore broaden the range of microemulsion existence. A very rigid surfactant film will not enable existence of bicontinuous structures which will impede the range of existence. Besides microemulsions, structural examinations can reveal the existence of regular emulsions, anisotropic crystalline hexagonal or cubic phases, and lamellar structures depending on the ratio of the components.The internal structure of a microemulsion vehicle is very important for the diffusivity of the phases, and thereby also for the diffusion of a drug in the respective phases. Researchers have been trying zealously to understand the complicated phase behaviour and the various microstructures encountered in the microemulsion systems [14].

Components of Microemulsion Formulations

A large number of oils and surfactants are available which can be used as components of microemulsion systems but their toxicity, irritation potential and unclear mechanism of action limit their use. One must choose materials that are biocompatible, non-toxic, clinically acceptable, and use emulsifiers in an appropriate concentration range that will result in mild and non-aggressive microemulsions.

Divided into three they are

- Oil phase
- Surfactants
- Co-surfactants

1. Oil Phase

The oil component influences curvature by its ability to penetrate and hence swell the tail group region of the surfactant monolayer. Short chain oils penetrate the tail group region to a greater extent than long chain alkanes, and hence swell this region to a greater extent, resulting in increased negative curvature (and reduced effective HLB) [15]. Saturated (for example, lauric, myristic and capric acid) and unsaturated fatty acids (for example, oleic acid, linoleic acid and linolenic acid) have penetration enhancing property of their own and they have been studied since a long time. Fatty acid esters such as ethyl or methyl esters of lauric, myristic and oleic acid have also been employed as the oil phase.

Lipophilic drugs are preferably solubilized in o/w microemulsions. The main criterion for selecting the oil phase is that the drug should have high solubility in it. This will minimize the volume of the formulation to deliver the therapeutic dose of the drug in an encapsulated form.

2. **Surfactants**

The surfactant chosen must be able to lower the interfacial tension to a very small value which facilitates dispersion process during the preparation of the microemulsion and provide a flexible film that can readily deform around the droplets and be of the appropriate lipophilic character to provide the correct curvature at the interfacial region. It is generally accepted that low HLB surfactants are favoured for the formulation of w/o microemulsion, whereas surfactants with high HLB (>12) are preferred for the formation of o/w microemulsion. Surfactants having HLB greater than 20 often require the presence of cosurfactants to reduce their effective HLB to a value within the range required for microemulsion formation.

3. Cosurfactants

In most cases, single-chain surfactants alone are unable to reduce the o/w interfacial tension sufficiently to enable a microemulsion to form [16]. The presence of cosurfactants allows the interfacial film sufficient flexibility to take up different curvatures required to form microemulsion over a wide range of composition [15]. If a single surfactant film is desired, the lipophilic chains of the surfactant should be sufficiently short, or contain fluidizing groups (e.g. unsaturated bonds). Short to medium chain length alcohols (C3-C8) are commonly added as cosurfactants which further reduce the interfacial tension and increase the fluidity of the interface.

Choice of excipients

From biocompatibility consideration, the choice of excipients is restricted. Pharmaceutically accepted oils tend to be more polar and of much higher molecular weight than the more commonly used aliphatic or aromatic oils for non-pharmaceutical microemulsion. Usually, the oil which has maximum solubilizing potential for the drug is selected for the formulation of the microemulsion in order to achieve maximal drug loading. oils with long hydrocarbon chains (or high molecular volume) such as olive, peanut, soybean, canola and sunflower are difficult to microemulsify, whereas oils with shorter (or low molecular volume) such as medium chain triglycerides (MCT), medium chain mono- and diglycerides are easier to microemulsify. The choice of oil is often a compromise between solubility of the drug in the oil and microemulsification. But, the capacity of solubilizing lipophilic moieties usually increases with the chain length of the oil. Amongst the various oils, mono and diglycerides are preferred for oral delivery due to their ability to enhance permeation across the biological membranes, whereas for parenteral administration MCTs and fatty acid esters are preferred53. Triglycerides and esters of fatty acids, isopropyl myristate (IPM), ethyl oleate and oils of plant origin (corn, cottonseed, orange, clove, peppermint, eucalyptol and coconut) are also used as the oil phase to prepare pharmaceutical microemulsions for use through different routes of *in vivo* administration.

Choice of surfactant is crucial for the formulation of microemulsions, because preparation of a microemulsion generally requires the use of moderate to high concentration of surfactant. Even

pharmaceutically accepted surfactants have adverse side effects above the recommended concentration11. Naturally occurring surfactants, lecithin and related phospholipids are preferred over synthetic surfactants, but they always need a co-surfactant because of the strongly lipophilic nature and its tendency to form rigid lamellar phase.

Method of Preparation

1. Phase Titration Method

Microemulsions are prepared by the spontaneous emulsification method (phase titration method) and can be depicted with the help of phase diagrams. Construction of phase diagram is a useful approach to study the complex series of interactions that can occur when different components are mixed. Microemulsions are formed along with various association structures (including emulsion, micelles, lamellar, hexagonal, cubic, and various gels and oily dispersion) depending on the chemical composition and concentration of each component. The understanding of their phase equilibria and demarcation of the phase boundaries are essential aspects of the study. As quaternary phase diagram (four component system) is time consuming and difficult to interpret, pseudo ternary phase diagram is often constructed to find the different zones including microemulsion zone, in which each corner of the diagram represents 100% of the particular component Fig. (**2**). The region can be separated into w/o or o/w microemulsion by simply considering the composition that is whether it is oil rich or water rich. Observations should be made carefully so that the metastable systems are not included. The methodology has been comprehensively discussed by Shafiq-un-Nabi *et al.*

2. Phase Inversion Method

Phase inversion of microemulsions occurs upon addition of excess of the dispersed phase or in response to temperature. During phase inversion drastic 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. For non-ionic surfactants, this can be achieved by changing the temperature of the system, forcing a transition from an o/w microemulsion at low temperatures to a w/o microemulsion at higher temperatures (transitional phase inversion). During cooling, the system crosses a point of zero spontaneous curvature and minimal surface tension, promoting the formation of finely dispersed oil droplets. This method is referred to as phase inversion temperature (PIT) method. Instead of the temperature, other parameters such as salt concentration or pH value may be considered as well instead of the temperature alone. Additionally, a transition in the spontaneous radius of curvature can be obtained by changing the water volume fraction. By successively adding water into oil, initially water droplets are formed in a continuous oil phase. 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 locus. Short-chain surfactants form flexible monolayer's at the o/w interface resulting in a bicontinuous microemulsions at the inversion point.

Characterization of Microemulsion

The formulated microemulsions were then recognized and characterized on the basis of their physical properties, which can not only explain the performance of the system but also help in modifying their performance attributes. The optical properties of the micro droplets, their behavior in a gravitational field and rheological behavior easily differentiate them from macro droplets.

Transparency/Translucency

The droplets of the microemulsions being smaller than ¼ th the wavelength of visible light, permit white light to pass through the dispersed system making it transparent or translucent. The microemulsion systems were inspected for optical transparency and homogeneity by usual observation against strong light. The systems were also checked for the presence of undissolved drug or other solid ingredient.

Globule Size Analysis of the Microemulsion

The average globule size and polydispersity index of the medicated microemulsion were determined by the photon correlation spectroscopy. Measurements were carried at an angle of 90° at 25 °C. Microemulsion was diluted with double distilled water to ensure that the light scattering intensity was within the instrument's sensitivity range. Double distilled water was filtered through 0.45µ membrane filters prior to globule size determination.

Optical Birefringence

Microemulsion was placed between two polarizing plates in a series and then observed for light transmittance. After this, one of the plates was rotated relative to the other through 90o (crossed polarizer's) and then examined.

Centrifugation

This technique helps to determine behavior of small particles in gravitational field i.e., their separation rate is quite simple and inexpensive providing a rapid full-proof identification of the system as microemulsion. Microemulsion systems were subjected to centrifugation at 3000 rpm for 30 minutes and then examined for any phase separation.

Solubility Analysis

An excess amount of drug was added in test tube containing 5 ml of IPP and IPP-microemulsion. The tubes were kept on mechanical water bath shaker (Neolab) at 320C for 72 h. The suspension was filtered through membrane filter [0.45µ] .The filtrate was diluted with methanol and drug concentration was determined spectrophotometrically at 261 nm. Identical method was followed to determine solubility of drug in LLP and LLP –microemulsion.

***In Vitro* Evaluation for Screening of Microemulsion**

The diffusion of fluconazole from the microemulsion was investigated across the excised rat skin using the same diffusion cell model (Keshary-Chien type Jadhav *et al*. International Journal of Advances in Pharmaceutical Sciences 1 (2010) [21] diffusion cells) and the same method that was used for in vitro inherent flux study. Full thickness abdominal skin of albino rats (125-150g) was used. The dermal surface was carefully cleaned to remove subcutaneous tissues and fats without damaging the epidermal surface. One-gram of drug formulation was placed on the skin surface in the donor compartment. The amount of drug diffused across the skin was estimated by analyzing the drug concentration within receptor medium using HPLC method. Average values of three readings of in vitro permeation data were calculated and the average cumulative amount of drug permeated per unit surface area of the skin was plotted versus time.

The slope of the linear portion of the plot was calculated as flux Jss (µg/cm2/h) 12 and the permeability coefficient was calculated using following formula

Kp = Jss

Cv

Where Kp is permeability coefficient and Cv is total amount of drug.

The drug fluxes from IPP microemulsions were compared with the fluxes from LLP microemulsions.

Construction of Phase Diagrams

Water titration method was adopted to locate microemulsion zone. Pseudoternary phase diagrams were constructed to examine the formation of water in oil microemulsions using four components. The four component system consisted of; (1) Oil (medium-chain fatty acid–based triglyceride, oleic acid); (2) a co-surfactant (polyethylene glycol); (3) a high-HLB surfactant (Cremophor EL); and (4) double-distilled water (aqueous phase).

MICROEMULSIONS IN DRUG DELIVERY

During the last two decades, microemulsions have been extensively researched because of their tremendous potential in many

applications. The role of microemulsions in drug delivery and the patents granted shall be discussed comprehensively herein.

Oral Delivery

The development of the effective oral delivery systems has always been the main goal because drug efficacy can be severely limited by instability or poor solubility in the gastrointestinal fluid. Biopharmaceutical Classification System (BCS) is a useful guidance by US FDA and it takes into account contributions of three major factors, dissolution, solubility, and intestinal permeability, which affect oral drug absorption. According to the BCS, drug substances are classified as follows

Class I - High Permeability, High Solubility

Class II - High Permeability, Low Solubility

Class III - Low Permeability, High Solubility

Class IV - Low Permeability, Low Solubility

Microemulsions have the potential to enhance the solubilization of the poorly soluble drugs and overcome the dissolution related bioavailability problems. This is particularly important for the BCS class II or class IV drugs. The successful formulation of such drugs is highly dependent on the performance of the formulated product. Microemulsions act as super solvent of these drugs and can be optimized to ensure consistent bioavailability.

Crison *et al.* taught a self-microemulsifying formulation for increasing the bioavailability of a drug which included oil/ lipid material, a surfactant, and a hydrophilic co-surfactan. HLB of hydrophilic co-surfactant was greater than 8. The self-microemulsifying formulation could also include the addition of an aqueous solvent such as triacetin. They had found that a more hydrophilic co-surfactant not only increased the dissolution of poorly water-soluble drugs but, that it also increased their *in vivo* bioavailability.

Protein and Peptide Drug Delivery

Numerous peptide and proteins have been identified for use as novel therapeutic agents. With increase in the understanding of their structure and mechanism, recent research has shifted to biotechnological products [20]. Changing scenario and increased market competitiveness is pressurizing companies to address significant protein delivery issues already at late discovery and early development stages. However, in spite of tremendous advances in peptide and protein development, their delivery is limited to systemic route. This is due to their low oral bioavailability which can be ascribed to their inactivation by gastrointestinal enzymes and poor permeability of the intestinal mucosa. To circumvent this, microemulsions have been developed as smart systems and patented for the oral delivery of protein and peptide drugs.

Cyclosporine Delivery

Cyclosporine delivery has remained a challenge for the formulation scientists. It is an immunosuppressive agent and is widely used in recipients of organ transplants and in various autoimmune diseases. It exerts potent immunosuppressive activity by inhibiting the growth and differentiation of T cells. The inherent insolubility of the cyclosporine provides the major hurdle for the low and variable bioavailability and there is variability in inter- and intra-patient dose response and low formulation stability during storage.

Parenteral Delivery

The formulation of lipophilic and hydrophobic drugs into parenteral dosage forms has proven to be difficult. O/w microemulsions are beneficial in the parenteral delivery of sparingly soluble drugs where the administration of suspension is not desirable. They provide a means of obtaining relatively high concentration of these drugs which usually requires frequent administration. Other advantages are that they exhibit a higher physical stability in plasma than liposomes or other vesicles and the internal oil phase is more resistant against drug leaching. Several sparingly soluble drugs have been formulated into o/w microemulsion for parenteral delivery [21]. Microemulsions can also be used as intravenous delivery systems for the fat soluble vitamins and lipids in parenteral nutrition [21].

Topical Delivery

Microemulsion systems are now being investigated zealously for topical delivery which is evident from the numerous publications coming up every year. They have been reported to enhance the transdermal permeation of drugs significantly compared to conventional formulations such as solutions, gels or creams [22]. They are able to incorporate both hydrophilic (5-fluorouracil, apomorphine hydrochloride, diphenhydramine hydrochloride, tetracaine hydrochloride, methotrexate) and lipophilic drugs (estradiol, finasteride, ketoprofen, meloxicam, felodipine, triptolide) and enhance their permeation. Since the microemulsion is a multicomponent system and its formation requires high surfactant concentration, the skin irritation aspect must be considered especially when they are intended to be applied for a longer period.

Ophthalmic Delivery

In conventional ophthalmic dosage forms, water soluble drugs are delivered in aqueous solution while water insoluble drugs are formulated as suspensions or ointments. Low corneal bioavailability and lack of efficiency in the posterior segment of ocular tissue are some of the serious drawbacks of these systems. Recent research efforts have therefore focused on the development of new and more effective delivery systems. Microemulsions have emerged as a promising dosage form for ocular use [23].

Nasal Delivery

Microemulsions are now being studied as a delivery system to enhance uptake across nasal mucosa. Addition of a mucoadhesive polymer helps in prolonging the residence time on the mucosa. Nasal route for administration of diazepam might be a useful approach for the rapid onset of action during the emergency treatment of status epilepticus.

Periodontal Delivery

Periodontal disease is a collective term for a number of progressive oral pathological afflictions like inflammation and degeneration of the gums, periodontal ligaments, cementum and its supporting bone. It is a major cause of tooth loss. The invention of Brodin *et al*. included a novel pharmaceutical composition comprising local anesthetic in oil form, surfactant, water and optionally a taste masking agent [24].

New approach of Drug Targeting

Drug targeting has evolved as the most desirable but elusive goal in drug delivery. By altering the pharmacokinetics and biodistribution of drugs and restricting their action to the targeted tissue increased drug efficacy with concomitant reduction of their toxic effects can be achieved. Submicron size range of these systems confers excellent opportunities to overcome the physiological barriers and enables efficient cellular uptake followed by intracellular internalization.

Cellular Targeting

Nucleic acids delivered to cells are promising therapeutics. The invention of Monahan *et al.* included insertion of nucleic acid into a reverse micelle for cell delivery [25]. They referred w/o microemulsions to as reverse micelles. The reverse micelle had the property to compact the nucleic acid for easier delivery. To further enhance the delivery, other molecules such as a surfactant having a disulfide bond or a polyion might be added to the nucleic acid-micelle complex.

Tumour Targeting

Shiokawa and coworkers reported a novel microemulsion formulation for tumor targeted drug carrier of lipophilic antitumour antibiotic aclacinomycin A (ACM) [26]. Their findings suggested that a folate-linked microemulsion is feasible for tumour targeted ACM delivery. The study showed that folate modification with a sufficiently long PEG chain on emulsions is an effective way of targeting emulsion to tumour cells.

Brain Targeting

Intranasal administration confers a simple, practical, cost effective, convenient and noninvasive route of administration for rapid drug delivery to the brain. It allows a direct transport of drugs to the brain circumventing the brain barriers [27]. Vyas *et al*. prepared Mucoadhesive microemulsion for an antiepileptic drug clonazepam [28].

CURRENT & FUTURE DEVELOPMENTS

The full potential of microemulsion systems is yet to be realized. A lot of innovations are expected to come in the field of microemulsion technology. A recent patent assigned to Novartis AG was concerned with the delivery of cyclosporines (excluding cyclosporine A) [29]. It included microemulsions and microemulsion pre-concentrate composition comprising of a hydrophilic component, lipophilic component containing cyclosporine and hydrophilic surfactant. The hydrophilic phase comprised of C1-5 alkyl or tetrahydrofurfuryl di- or partial-ether of a low molecular weight mono- or poly-oxy-alkanediol (e.g. Transcutol® , Glycofurol®); or 1,2-propyleneglycol. The composition upon dilution with adequate water spontaneously produced an o/w microemulsion having an average particle size of less than about 0.15 microns. The compositions permitted the preparation of solid, semi-solid and liquid preparations containing a cyclosporine in sufficiently high concentration which allowed convenient oral administration while at the same time achieving improved efficacy. In addition to oral drug delivery, a lot of topical products employing the microemulsion technology are likely to emerge. This is significant not only from the view point of drug delivery but also from the huge and lucrative cosmetic market prospects. the current scientific interest seems to be directed at recognizing its full potential as a novel drug delivery tool.

CONCLUSION

Microemulsions are commercially feasible, simple and convenient novel vehicles for delivery of medicaments which can enhance drug absorption with reduced systemic side effects. They can be used to optimize drug targeting without a concomitant increase in systemic absorption. Appropriate excipient selection and safety evaluation especially of the cosurfactants is crucial in the formulation of microemulsions. They can be potential drug delivery systems for the delivery of more than one medicament simultaneously.

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