



## Investigation of Microemulsion as a Potential Carrier for Advanced Transdermal Delivery: An Overview

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### ABSTRACT

Microemulsions are clear, transparent, thermodynamically stable dispersions of oil and water, stabilized by an interfacial film of surfactant frequently in combination with a co-surfactant. Microemulsion formulation has been used for the delivery of hydrophilic as well as lipophilic drugs because of its improved drug solubilization capacity, long shelf life, ease of preparation and improved bioavailability. These systems are currently of interest to the pharmaceutical scientist because of their unique characteristics and considerable potential to act as drug delivery carrier by incorporating a wide range of drug molecules. Preparing a pharmaceutically acceptable microemulsion demands a clear understanding of the micro-emulsion structure, phase behavior, factors leading to its thermodynamic stability, factors influencing drug release from the formulation, requirements of ideal microemulsion excipients, and the potential uses and limitations of the microemulsion system. This review highlights potential of Microemulsion as a drug delivery carrier on the basis of various research works on Microemulsion based system.

**Keywords:** Microemulsions, Surfactants, Cosurfactants, Thermodynamic stability, Phase behavior, Novel carriers.

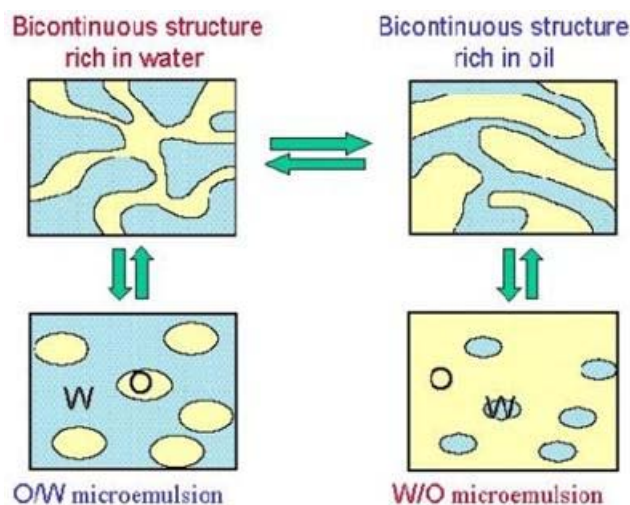
### INTRODUCTION

Microemulsion<sup>1-5</sup> is homogeneous, transparent, thermodynamically stable dispersions of water and oil, stabilized by a surfactant, usually in combination with a cosurfactant and whose diameter is in the range of 10-140 nm. microemulsions are being extensively investigated as drug delivery carriers. Much of the interest in the use of microemulsions as drug delivery carrier arises from their unique physical properties, particularly, their thermodynamic stability and ease of preparation.

### History, definitions and concepts

Hoar and Schulman had already noticed in 1943 that by titrating a milky emulsion (a mixture of water, oil, and surfactant) with hexanol, a clear single-phase and stable solution was formed<sup>6</sup>. Schulman and associates also coined the term microemulsion that holds up to this day<sup>7</sup>. The definition has changed slightly through the years, but the general concepts are still intact. Most scientists use a general and broad definition for microemulsion as, a system of water, oil, and one or more surfactant (or amphiphile) which is a single optically isotropic and thermodynamically stable solution. It is well established today that microemulsions can appear in at least three major microstructures: water-in-oil (w/o), oil-in-water (o/w) and bicontinuous structure. Microemulsions have very high surface areas and, therefore, it is obvious that they can incorporate, in their core or at the interface, large quantities of molecules that are usually insoluble in the continuous phase. The molecules that are incorporated at the interface are solubilized rather than dissolved, and, therefore, microemulsion efficiency is measured based on the solubilization capacity of guest molecules (i.e. drugs. For a microemulsion to exhibit drug

delivery properties, the existence of microstructures in the mixture must be clearly demonstrated. The choice of type of microemulsion for particular therapy depends on the route of administration and intended target organ.



**Figure 1:** Diagrammatic representation of different types of Microemulsion systems: (a) w/o ME, (b) o/w ME, and (c) Bicontinuous ME.

The main difference between emulsions and microemulsions lies in their size and shape of the droplets that are dispersed in the continuous phase. Because the size of the particles is much smaller than the wavelength of visible light, microemulsions are transparent and their structure cannot be observed through an optical microscope. Microemulsions are isotropic solutions of oil and water and are prepared using a high surfactant concentration of around 40 percent under gentle stirring or shaking.

**Table 1:** Difference between Microemulsion and Macroemulsion<sup>8</sup>

Property	Microemulsion	Macroemulsion
Appearance	Transparent	Cloudy
Optical Isotropy	Isotropic	Anisotropic
Interfacial tension	Ultra low	High
Microstructure	Dynamic (interface is continuously and spontaneously fluctuating)	Static
Droplet size	20-200 nm	> 500 nm
Preparation	Facile preparation, relatively lower cost for commercial production	Require a large input of energy, higher cost
Viscosity	Low viscosity	Higher viscosity

These versatile systems are currently of great technological and scientific interest to the researchers because of their potential to incorporate a wide range of drug molecules (hydrophilic and hydrophobic) due to the presence of both lipophilic and hydrophilic domains. These adaptable delivery systems provide protection against oxidation, enzymatic hydrolysis and improve the solubilization of lipophilic drugs and hence enhance their bioavailability. In addition to oral and intravenous delivery, they are amenable for sustained and targeted delivery through ophthalmic, dental, pulmonary, vaginal and topical routes.

Microemulsions are experiencing a very active development as reflected by the numerous publications and patents being granted on these systems.

### THEORIES OF MICROEMULSION FORMATION

Three approaches have been used to explain microemulsion formation and stability. They are as follows-

1. Interfacial or mixed film theories.
2. Solubilization theories.
3. Thermodynamic treatments.

The free energy of microemulsion formation can be considered to depend on the extent to which surfactant lowers the surface tension of the oil water interface and change in entropy of the system such that,

$$G_f = \gamma a - TS$$

Where,  $G_f$  = free energy of formation

$A$  = change in interfacial area of microemulsion

$S$  = change in entropy of the system

$T$  = temperature

$\gamma$  = surface tension of oil water interphase

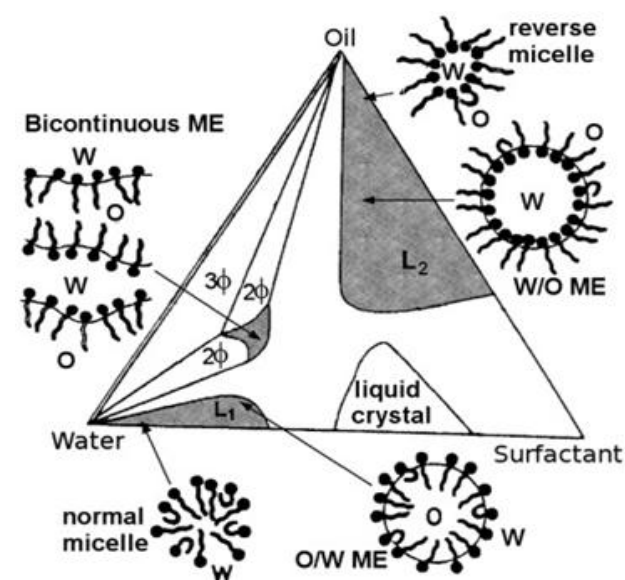
It should be noted that when a microemulsion is formed the change in "A" is very large due to the large number of very small droplets formed. In order for a microemulsion to be formed (transient) negative value of  $\Delta G$  was required, it

is recognized that while value of  $\Delta G$  is positive at all times, it is very small and it is offset by the entropic component. The dominant favorable entropic contribution is very large dispersion entropy arising from the mixing of one phase in the other in the form of large number of small droplets. However there are also expected to be favorable entropic contributions arising from other dynamic processes such as surfactant diffusion in the interfacial layer and monomer-micelle surfactant exchange. Thus a negative free energy of formation is achieved when large reductions in surface tension are accompanied by significant favorable entropic change. In such cases, microemulsion is spontaneous and the resulting dispersion is thermodynamically stable<sup>9-10</sup>

### TYPES OF MICROEMULSION SYSTEMS

According to Winsor, there are four types of microemulsion phases exists in equilibria, these phases are referred as Winsor phases<sup>11-12</sup>. They are,

1. **Winsor I:** With two phases, the lower (o/w) microemulsion phases in equilibrium with the upper excess oil.
2. **Winsor II:** With two phases, the upper microemulsion phase (w/o) microemulsion phases in equilibrium with lower excess water.
3. **Winsor III:** With three phases, middle microemulsion phase (o/w plus w/o, called bicontinuous) in equilibrium with upper excess oil and lower excess water.
4. **Winsor IV:** In single phase, with oil, water and surfactant homogenously mixed.



**Figure 2:** A ternary phase diagram portraying various structures a) o/w microemulsion; b) w/o microemulsion; c) bicontinuous microemulsion; d) and e) various dispersions

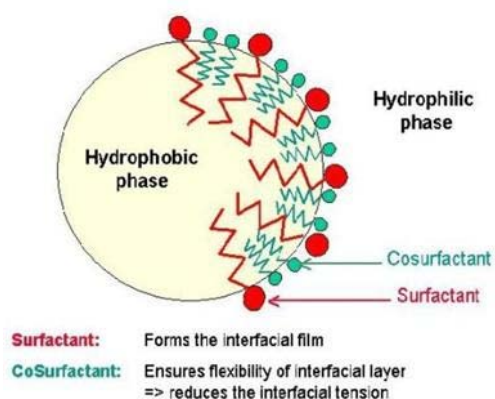
### Advantages of Microemulsion over Other Dosage Forms

1. Increase the rate of absorption.
2. Eliminates variability in absorption.

3. Helps solublize lipophilic drug.
4. Provides a aqueous dosage form for water insoluble drugs.
5. Increases bioavailability.
6. Various routes like topical, oral and intravenous can be used to deliver the product.
7. Rapid and efficient penetration of the drug moiety.
8. Helpful in taste masking.
9. Provides protection from hydrolysis and oxidation as drug in oil phase in o/w microemulsion is not exposed to attack by water and air.
10. Liquid dosage form increases patient compliance.
11. Less amount of energy requirement

### COMPONENTS OF MICROEMULSION SYSTEM

A large number of oils and surfactant are available but their use in the microemulsion formulation is restricted due to their toxicity, irritation potential and unclear mechanism of action. Oils and surfactant which will be used for the formulation of microemulsion should be biocompatible, non-toxic, clinically acceptable, and use emulsifiers in an appropriate concentration range that will result in mild and non-aggressive microemulsion. The emphasis is, excipients should be generally regarded as safe.



### Oil Phase

The oil component influences curvature by its ability to penetrate and swell the tail group region of the surfactant monolayer. As compare to long chain alkanes, short chain oil penetrate the tail group region to a greater extent and resulting in increased negative curvature (and reduced effective HLB). Following are the different oil are mainly used for the formulation of microemulsion:

1. Saturated fatty acid-lauric acid, myristic acid, capric acid
2. Unsaturated fatty acid-oleic acid, linoleic acid, linolenic acid
3. Fatty acid ester-ethyl or methyl esters of lauric, myristic and oleic acid.

The main criterion for the selection of oil 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.

### Surfactants

The role of surfactant in the formulation of microemulsion is to lower the interfacial tension which will ultimately facilitates dispersion process during the preparation of microemulsion and provide a flexible around the droplets. The surfactant should have appropriate lipophilic character to provide the correct curvature at the interfacial region. Generally, low HLB surfactants are suitable for w/o microemulsion, whereas high HLB (>12) are suitable for o/w microemulsion. Following are the different surfactants are mainly used for microemulsion-Polysorbate (Tween 80 and Tween 20), Lauromacrogol 300, Lecithins, Decyl polyglucoside (Labrafil M 1944 LS), Polyglyceryl-6-dioleate (Plurol Oleique), Dioctyl sodium sulfosuccinate (Aersol OT), PEG-8 caprylic/capril glyceride (Labrasol).

### Cosurfactants

Cosurfactants are mainly used in microemulsion formulation for following reasons:

1. They allow the interfacial film sufficient flexible to take up different curvatures required to form microemulsion over a wide range of composition.
2. Short to medium chain length alcohols(C3-C8) reduce the interfacial tension and increase the fluidity of the interface.
3. Surfactant having HLB greater than 20 often require the presence of cosurfactant to reduce their effective HLB to a value within the range required for microemulsion formulation. Following are the different cosurfactant mainly used for microemulsion:

Sorbitan monooleate, Sorbitan monosterate, Propylene glycol, Propylene glycol monocaprylate (Capryol 90), 2-(2-ethoxyethoxy)ethanol (Transcutol) and Ethanol.

### PREPARATION OF MICROEMULSION

Following are the different methods are used for the preparation of microemulsion.<sup>13</sup>

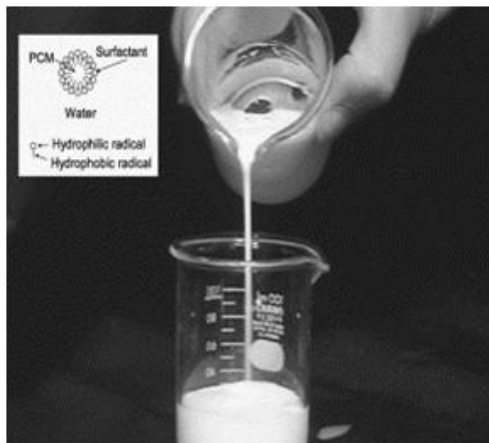
Phase inversion method

Phase titration method

#### Phase titration method

Microemulsions are prepared by the spontaneous emulsification method (phase titration method) and can be portrayed with the help of phase diagram. As quaternary phase diagram (four component system) is time consuming and difficult to interpret, pseudo ternary phase diagram is constructed to find out the different zones including microemulsion zone, in which each corner of the diagram represents 100% of the particular components. Pseudo-ternary phase diagrams of oil,

water, and co-surfactant/surfactants mixtures are constructed at fixed cosurfactant/surfactant weight ratios. Phase diagrams are obtained by mixing of the ingredients, which shall be pre-weighed into glass vials and titrated with water and stirred well at room temperature. Formation of monophasic/ biphasic system is confirmed by visual inspection. In case turbidity appears followed by a phase separation, the samples shall be considered as biphasic. In case monophasic, clear and transparent mixtures are visualized after stirring; the samples shall be marked as points in the phase diagram. The area covered by these points is considered as the microemulsion region of existence.



#### Phase inversion method

Phase inversion of microemulsion is carried out 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 ultimately affect drug release both *in vitro* and *in vivo*. 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 temperature to a w/o microemulsion at higher temperatures (transitional phase inversion). During cooling, the system crosses a point zero spontaneous curvature and minimal surface tension, promoting the formation of finely dispersed oil droplets. Apart from temperature, salt concentration or pH value may also be considered. A transition in the radius of curvature can be obtained by changing the water volume fraction. Initially water droplets are formed in a continuous oil phase by successively adding water into oil. 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.

#### EVALUATION OF MICROEMULSION

Evaluation of microemulsion is very challenging due to their small droplet size with fluctuating boundaries and complex structure. Following are different parameters are evaluated for the microemulsion:

**Phase behavior study** can be used to differentiate microemulsions from liquid crystals and coarse

emulsions. This is carried out by visual observations, phase contrast microscope and freeze fracture transmission electron microscope.

**Viscosity measurement** can indicate the presence of rod-like or worm-like reverse micelles. Conductivity measurement provide means of determining whether a microemulsion is oil-continuous or water-continuous, as well as providing means of monitoring percolation or phase inversion phenomena. Dielectric measurements are powerful means probing both the structural and dynamic features of microemulsion systems.

**Isotropic nature** of microemulsion and their optical clarity can be evaluated by spectroscopic techniques, particularly by comparison to conventional microemulsions. Pulse field gradient NMR has been used to measure self-diffusion coefficient of the various components and yield information on the mobility and microenvironment. Scatter methods such as dynamic and static light scattering (SANS) and small angle X-ray scattering (SAXS) as well as cryo transmission electron microscopy have been used to determining particle size of microemulsion.

#### APPLICATION OF MICROEMULSION IN DELIVERY OF DRUG

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 role of microemulsion as drug delivery system shall be discussed here below.

##### Oral delivery

The development of effective oral delivery systems has always been challenging to researchers because drug efficacy can be restricted by instability or poor solubility in the gastrointestinal fluid. Microemulsions have the potential to enhance the solubilization of poorly soluble drugs and overcome the dissolution related bioavailability problems. Due to the presence of polar, nonpolar and interfacial domains, hydrophilic drugs including macromolecules can be encapsulated with varying solubility. These systems have been protecting the incorporated drugs against oxidation, enzymatic degradation and enhance membrane permeability. Microemulsion formulation can be potentially useful to improve the oral bioavailability of poorly water soluble drugs by enhancing their solubility in gastrointestinal fluid<sup>14</sup>.

##### Parenteral delivery

The formulation of parenteral dosage form of lipophilic and hydrophilic drugs 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 required. 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 liposome's or other vehicles 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.

### Topical delivery

Topical administration of drugs can have advantages over other methods for several reasons, one of which is the avoidance of hepatic first-pass metabolism of the drug and related toxicity effects. Another is the direct delivery and targetability of the drug to affected areas of the skin or eyes. Now a day, there have been a number of studies in the area of drug penetration into the skin. They are able to incorporate both hydrophilic and lipophilic drugs and enhance their permeation. Since formation of microemulsion formation requires high surfactant concentration, the skin irritation aspect must be considered especially when they are intended to be applied for a longer period<sup>15</sup>. The following is a compilation of topical microemulsion formulations:

### Antifungal

Superficial mycoses usually respond to topical therapy. In the settling of eczema, topical antifungal agents such as ketoconazole are used to reduce the fungal infection caused by *Pityrosporum ovale* or *Malassezia furfur*. Antifungal agents e.g miconazole, ketoconazole, and itraconazole 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 conventional dosage forms<sup>16,17</sup>. Microemulsions of poorly water soluble antifungal drugs miconazole, ketoconazole, and itraconazole were designed and developed using either mineral oil or olive oil as an oil phase<sup>18</sup>. Various combinations of surfactant and cosurfactant were used, including Labrafil M 1944 CS and Pluro Oleique (1:1); Labrafil M 1944 CS and Pluro Oleique (1:2); or Labrafil M 1944 CS, Capmul MCM C-8, Pluro Oleique, and dehydrated ethyl alcohol (3:3:1:1).

Microemulsions of poorly water-soluble antifungal agents were successfully developed with *in vitro* release rates comparable to that of the gel formulation. The results of the work done on miconazole nitrate formulated as positively charged microemulsions indicate optimized drug targeting without a concomitant increase in systemic absorption. L-alanine benzyl ester, an ester of a natural amino acid, is an appropriate ionic charge-inducing agent<sup>19</sup>. Microemulsion based gels for vaginal delivery of clotrimazole and fluconazole were developed and compared with the marketed clotrimazole gel (Candid-V® gel) by *in vitro* methods. These microemulsion based gels showed significantly higher *in vitro* bioadhesion,

antifungal activity as compared to that of Candid-V® gel. Fluconazole microemulsion based gel did not exhibit vaginal irritation<sup>20,21</sup>

### 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, microemulsion-based 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. Thus, it can be concluded that microemulsion based hydrogel could be a promising vehicle for topical delivery of penciclovir<sup>22</sup>. Acyclovir containing microemulsion-based formulations for topical delivery were developed using isopropyl myristate/Captex 355/Labrafac as an oil phase, Tween 20 as surfactant, Sp a n 20 as cosurfactant, and (1:3) as an aqueous phase. Transcutol, eucalyptus oil, and peppermint oil were used as permeation enhancers. *In vitro* permeation studies through mice skin were performed using Franz diffusion cells. The optimum formulation containing 2.5% Transcutol as the penetration enhancer showed 1.7-fold enhancement in flux and permeation coefficient as compared to marketed cream and ointment formulation. *In vivo* antiviral studies performed in female mice against induced herpes simplex virus infection indicated that a single application of microemulsion formulation containing 2.5% Transcutol, 24 hours post-injection resulted in complete suppression of development of herpetic skin lesions.

### 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<sup>23</sup>. 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. Dialysis membrane experiments showed decreasing permeability to AZA-Na, and this was related to its partition at the microemulsion interface. The results suggested that microemulsions containing AZA-Na could be used to optimize drug targeting in acne treatment<sup>24</sup>. To increase the solubility of azelaic acid in the dispersed oil phase of microemulsion containing polysorbate 20, butanol, decanol:dodecanol (2/1) and water, the pH of aqueous phase was lowered and propylene glycol was added. An increased partitioning into the lipophilic phase was noted as propylene glycol concentration was increased. Microemulsion thus provided a vehicle in



which azelaic acid was dissolved rather than suspended as in a cream. Moreover, reservoir effect achieved by partitioning into the oil could prolong its release over several hours. It showed a 10 fold increase in the amount of drug released (upto 27-30% of initial amount) from the microemulsion when compared to a cream clinically used in treatment of skin disorders<sup>25</sup>.

### 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. In animals, topical application of alpha-tocopherol has shown to exert photoprotective effects by reducing the number of sunburn cells, UV B induced damage and inhibiting photocarcinogenesis. An o/w or w/o microemulsion of vitamin E delivered the vitamin predominantly to the epidermis avoiding accumulation in organs other than the skin. The cream or lotion preparations of the same amount of vitamin results in excessive accumulation in the organs<sup>26</sup>. Newer studies show that combined applications of various antioxidants can increase their potency as compared with a single antioxidant alone. Branka Rozman et al<sup>27</sup> have developed a temperature-sensitive microemulsion gel as an effective and safe delivery system suitable for simultaneous topical application of a hydrophilic vitamin C and a lipophilic vitamin E. By changing water content of liquid o/w microemulsion, a gel like microemulsion with temperature sensitive rheological properties was formed. The temperature-driven changes in its microstructure were confirmed by rotational rheometry, viscosity measurements and droplet size determination. The release studies have shown that the vitamin release at skin temperature from gel like microemulsion were comparable to those from o/w microemulsion and were much faster and more complete than from o/w microemulsion conventionally thickened with polymer (carbomer). Non-thickened (o/w, w/o and gel-like) and thickened (with colloidal silica) microemulsions were studied as carriers for vitamin C and E using reconstructed human epidermis (RHE). The amounts of these vitamins accumulated in and permeated across the RHE were determined, together with factors affecting skin deposition and permeation. Notable differences were observed between formulations. The absorption of vitamins C and E in RHE layers was in general enhanced by microemulsions and the vitamins incorporated in the outer phase of the microemulsion exhibited greater absorption than that when vitamins were in the inner phase.

Addition of thickener enhanced the deposition of vitamins E and C in the RHE<sup>28</sup>. Various delivery systems of alpha-tocopherol (1%) were formulated, which included simple solution, gels, emulsions, and microemulsions. The hydroalcoholic gel delivered significantly higher amounts of alpha-tocopherol into the receptor than the other gels used. A microemulsion containing isopropyl myristate

emerged as the best delivery system for alpha-tocopherol amongst all the systems studied<sup>29</sup>. Microemulsions of w/o and o/w type for topical application containing sodium ascorbyl phosphate (hydrophilic derivative of ascorbic acid) were formulated and compared with topical application of ascorbyl palmitate which is a lipophilic derivative of vitamin C. To obtain liquid microemulsions appropriate for topical application, their viscosity was increased by adding thickening agents. Colloidal silica 4% (w/w) was chosen as a suitable thickening agent for w/o microemulsions and 0.5% (w/w) xanthan gum for the o/w microemulsions. The presence of thickening agent and the location of sodium ascorbyl phosphate in the microemulsion influenced the *in vitro* drug release profiles. When incorporated in the internal aqueous phase, sustained release profiles were observed. This study confirmed microemulsions as suitable carrier systems for topical application of sodium ascorbyl phosphate<sup>30</sup>. Spiclin et al.,<sup>31</sup> studied the stability of o/w and w/o type of

microemulsions for topical use containing ascorbyl palmitate and sodium ascorbyl phosphate which are derivatives of ascorbic acid that differ in stability and hydrophilic and lipophilic properties. The stability of the less stable derivative ascorbyl palmitate was tested under different conditions to evaluate the influence of initial concentration, location in microemulsion, dissolved oxygen and storage conditions. High concentrations of ascorbyl palmitate reduced the extent of its degradation. In contrast, sodium ascorbyl phosphate was stable in both types of microemulsion and was shown to be convenient as an active ingredient in topical preparations. In the case of ascorbyl palmitate, long-term stability in selected microemulsions was not adequate. Investigation on the amphiphilic antioxidant ascorbyl palmitate and its effectiveness against free radical formation was proven by Polona Jurkovic *et al*<sup>32</sup>. When applied on the skin, ascorbyl palmitate decreased the level of formation of free radicals. Its effectiveness depended significantly on the carrier system, the type of microemulsion and its concentration while the time of application had no influence on its effectiveness. Oil in water microemulsions delivered ascorbyl palmitate to the skin significantly better than water in oil microemulsions. In both types of microemulsions, the effectiveness increased at higher concentrations of ascorbyl palmitate. In order to develop alternative formulations for topical administration of retinoic acid, Michele Trotta *et al*<sup>33</sup> evaluated microemulsions as delivery vehicles. Oil in water and water in oil microemulsion formulations were prepared using water, isopropyl myristate, lecithin, caprylyl-capryl glucoside and ethanol or 1,2 hexanediol. The results suggested that o/w microemulsions containing a counter ion can be used to optimise drug targeting without a concomitant increase in systemic absorption.



## 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. They are well suited for the preparation of various cosmetic products such as moisturizing and soothing agents, sunscreens, antiperspirants, body cleansing agents, hair conditioners and after shave formulations. Microemulsions are also suitable in perfumery so as to minimize the quantity of organic solvents.<sup>34</sup>

## Ophthalmic delivery

In conventional ophthalmic dosage forms, water soluble drugs are delivered in aqueous solution while water insoluble drugs are formulated as suspension or ointments. Low corneal bioavailability and lack of efficiency in the posterior segment of ocular tissue are some of the serious problem of this systems. Microemulsions have emerged as a promising dosage form for ocular use.

## Nasal delivery

Recently, microemulsions are being studied as a delivery system to enhance uptake of drug through nasal mucosa. In addition with mucoadhesive polymer helps in prolonging residence time on the mucosa<sup>35</sup>.

## Drug targeting

Drug targeting to the different tissues has evolved as the most desirable goal of drug delivery. By altering 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. Shiohawa *et al.* reported a novel microemulsion formulation for tumor targeting of lipophilic antitumor antibiotic aclarinomyacin A(ACM). They reported that a folate-linked microemulsion is feasible for tumour targeted ACM delivery. They also reported that folate modification with a sufficiently long PEG chain on emulsions is an effective way of targeting emulsion to tumour cells<sup>36</sup>.

## Research Work on Microemulsions

During the last one decade much research work has been done on microemulsions for various routes of drug administration. Due to their unique properties namely, ultraflow interfacial tension, large interfacial area, thermodynamic stability and the ability to solubilize otherwise immiscible liquids. Research work on microemulsions is summarized in Table 2.

Now a days, researcher work is focused on the production of safe, efficient and more compatible microemulsion constituents which will further enhance the utility of this novel delivery system.

**Table 2:** Research work on microemulsions

Drug name	Route	Purpose/result
Flurbiprofen <sup>37</sup>	Parenteral	Increased the solubility
Apomorphine HCL <sup>38</sup>	Transdermal	Increased the permeability
Ketoprofen <sup>39</sup>	Transdermal	Increased the permeability
Prilocaine-HCL <sup>40</sup>	Transdermal	Increased the solubility
Estradiol <sup>41</sup>	Transdermal	Improvement in solubilization
Aceclofenac <sup>42</sup>	Dermatological	Increased the solubility
Piroxicam <sup>43</sup>	Oral	Increased the solubility
Diclofenac <sup>44</sup>	Transdermal	Increased the permeability
Dexamethasone <sup>45</sup>	Topical ocular	Enhanced the bioavailability
Chloramphenicol <sup>46</sup>	ocular	Increased the solubility
Sumatriptan <sup>48</sup>	intranasal	Enhanced the bioavailability
Ibuprofen <sup>49</sup>	topical	Increased the solubility
Doxorubicin <sup>50</sup>	-	Increase the stability
Itraconazole <sup>51</sup>	parenteral	For better absorption
Timolol <sup>52</sup>	ophthalmic	For better absorption
Terbinafine <sup>53</sup>	Transdermal	Increased the permeability
Fenofibrate <sup>54</sup>	Self micro-emulsifying	Increased the solubility
Progesteron	dermal	Increased chemical stability

## 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 optimise 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. Microemulsions are readily distinguished from normal emulsions by their transparency, low viscosity and more fundamentally their thermodynamic stability. Drug delivery through microemulsions is a promising area for continued research with the aim of achieving controlled release with enhanced bioavailability and for drug targeting to various sites in the body.<sup>55-59</sup>

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