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## Investigating Application of Non Aqueous Microemulsion for Drug Delivery

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### Abstract

Non-aqueous system are well known as solvent or drug suspension vehicles and oleogels micro emulsion with no aqueous phase (anhydrous, non-aqueous oil-in-oil emulsion) have had relatively scant attention yet may have uses as drug reservoir as well as template for the preparation of microemulsion combination with a cosurfactant. Microemulsions have emerged as novel vehicles for drug delivery which allow sustained or controlled release for percutaneous, oral, 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. Delivery of drug using theses microemulsion through skin increase the local systemic delivery of the dug by different mechanism that make them suitable vehicles for the delivery of antifungal agent. Novel anhydrous micro emulsions, which may offer some advantages as depot or reservoir vehicles for lipophilic drugs in controlled delivery systems, intramuscular absorption.

**Keywords:** Microemulsions, Topical delivery, Surfactants, Cosurfactants.

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## INTRODUCTION

Microemulsions are thermodynamically stable system. The stability allows self-emulsification of the system whose properties are not dependent on the process followed.

Microemulsions act as supersolvents of drug. They can solubilize hydrophilic and lipophilic drugs including drugs that are relatively insoluble in both aqueous and hydrophobic solvents. This is due to existence of microdomains of different polarity within the same single-phase solution. The dispersed phase, lipophilic or hydrophilic (oil-in-water, O/W, or water-in-oil, W/O microemulsions) can behave as a potential reservoir of lipophilic or hydrophilic drugs, respectively. The drug partitions between dispersed and continuous phase, and when the system

comes into contact with a semi-permeable membrane, the drug can be transported through the barrier. Drug release with pseudo-zero-order kinetics can be obtained, depending on the volume of the dispersed phase, the partition of the drug and the transport rate of the drug. The mean diameter of droplets in microemulsions is below 0.22  $\mu\text{m}$ ; they can be sterilized by filtration. The small size of droplet in microemulsions e.g. below 100 nm, yields very large interfacial area, from which the drug can quickly be released into external phase when absorption (in vitro or in vivo) takes place, maintaining the concentration in the external phase close to initial levels. These microemulsions can carry both lipophilic and hydrophilic drugs because of thermodynamic stability, microemulsions are easy to prepare and require no significant energy contribution during preparation. Microemulsions have low viscosity compared to other emulsions. The use of microemulsion as delivery systems can improve the efficacy of a drug, allowing the total dose to be reduced and thus minimizing side effects. The formation of microemulsion is reversible. They may become unstable at low or high temperature but when the temperature returns to the stability range, the microemulsion reforms. Some disadvantages of microemulsion are large concentration of surfactant and co-surfactant necessary for stabilizing the nano droplets and limited solubilizing capacity for high melting substances. The surfactant must be nontoxic for using pharmaceutical application. Microemulsion stability is influenced by environmental parameter such as temperature and pH.

### Factors to Be Considered During Preparation of Microemulsion<sup>8</sup>

Three important conditions;

1. Surfactants must be carefully chosen so that an ultra low interfacial tension ( $< 10^{-3}$  mN/m) can be attained

at the oil/water interface which is a prime requirement to produce microemulsions.<sup>6</sup>

2. Concentration of surfactant must be high enough to provide the number of surfactant molecules needed to stabilize the micro droplets to be produced by an ultra low interfacial tension.<sup>6,7</sup>

3. The interface must be flexible or fluid enough to promote the formation of microemulsions.

### Structure of microemulsion

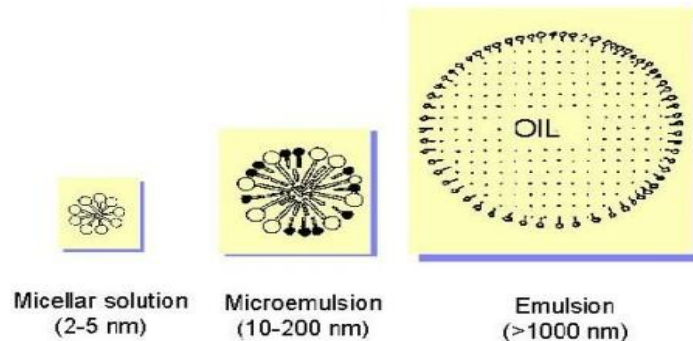


Figure 1: Structure of microemulsion

### Mechanism of microemulsion

Microemulsion has greatest challenge for topical drug delivery. Microemulsion containing drugs should penetrate into skin layers to ensure effective drug concentrations following topical administration. In topical administration, the entering of drugs to systemic circulation is prevented or minimized. Thus, the systemic adverse effects of drugs are avoided<sup>34</sup>. Besides, topical preparations have better patient compliance due to their non-invasiveness and, they can be self-administered.

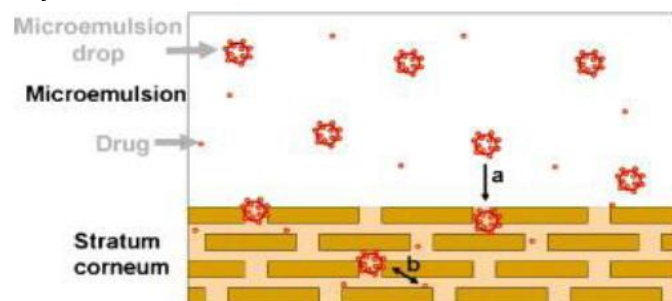


Figure 2: Mechanism of microemulsion

Micro emulsion have mobility of drug in the vehicle. This microemulsion improve its permeability release the drug from vehicle in to stratum corneum.

### Non aqueous microemulsion

The majority of studies of microemulsion utilize water as the polar solvent. Recently, attempt have been made to prepare and study nonaqueous microemulsion. In this effort, polar nonaqueous solvent have replaced the water and the preparation are essentially oil continuous. The nonaqueous microemulsions have bright and broad prospects in industrial applications.

They have been reported as a potentially useful media for organic reactions such as Diels–Alder and other stereoselective ones<sup>9,14</sup>. However the literature about the phase behavior of nonaqueous microemulsion is so far scanty. This provides the scope for further investigations on such system.

Non-aqueous microemulsions may be of pharmaceutical or cosmetic value if they are composed primarily of edible, non-toxic ingredients and can be formulated to exhibit a wide range of physical properties. Some possible uses might be as topical application bases for dermatological, particularly for labile drugs, as emollient bases for cosmetic preparations, or as nutrient preparations<sup>15,28</sup>. Yet it uses as drug reservoirs, as well as templates for the preparation of microspheres, nanoparticles and silicate microstructures<sup>19,21,22</sup>.

The invention of non aqueous emulsion is useful for drug delivery which largely overcomes the problems mentioned above with water-unstable and/or unsavory drugs. For example, a very palatable ibuprofen formulation can be made in which only one teaspoon contains a normal child's dose. "The emulsion contains a drug dissolved in a suitable non-aqueous internal phase solvent, such as propylene glycol, dispersed, with a suitable emulsifier such as lecithin in an alkyl fatty acid ester. Excipients such as sweeteners, flavoring agents and taste masking materials can also be included.

The main difference between non aqueous emulsion and non aqueous microemulsion are emulsion consist of roughly spherical droplets of one phase disperse in to the other having droplet diameter 1-20  $\mu$ m, (fig-3) but microemulsion are constantly involve between various structure ranging from droplet like swollen micelles to bicontinuous structure (fig-4) having droplet diameter 10-100nm. Most of emulsion are opaque (white) because bulk of their droplet is greater than wavelength of light and most oils have higher refractive indices than water. but microemulsion are transparent or translucent as their droplet diameter are less than one fourth of wavelength of light. Ordinary emulsion droplets, however small exist as individual entities until coalescence or Ostwald ripening occurs but in case of microemulsion droplet may disappear within a fraction of a second whilst another droplet forms spontaneously elsewhere in the system. Emulsion are stable for long periods of time, will ultimately undergo phase separation on standing to attain a minimum in free energy. They are kinetically stable thermodynamically unstable. They are lipophilic. But microemulsion are thermodynamically stable than macro emulsions and can have essentially infinite lifetime assuming no change in composition, temperature and pressure, and do not tend to separate.

They are on the borderline between lyophobic and lyophilic colloids.

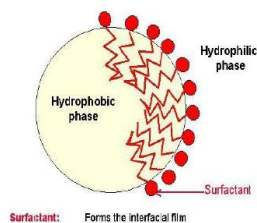


Figure-3

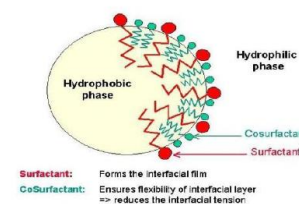


Figure-4

### Noteworthy contribution in developing non aqueous microemulsion

Hamill, R.D. were studied that emulsion stored at room temperature (25°C), and their droplet size, rheology and emulsion stability studied on days 1, 2, 4, 7, 14, 30 and 60. Droplet size was inversely related to surfactant concentration. Rheology studies with the Brookfield LVT viscometer revealed the existence of non-Newtonian pseudo viscous flow. The emulsions were very stable, as indicated by logarithmic graphs of viscosity and time.

Bauer, K. H. developed new vehicles based on non-aqueous emulsions. They may be classified as progress or supplementation to the conventional filling masses for soft gelatin capsules, but also for liquid or semi-solid hard gelatin capsule filling techniques. *In-vitro* dissolution rate studies exhibit a clear superiority of PEG filling masses about oil-wax bases, which show extremely slow release rates.

Dulak, M. P. *et al.* concluded that the anhydrous composition is exceptionally pleasing and cosmetically appealing when topically applied to the skin surface. It is surprisingly percutaneously absorbed and maintains the working ingredient stable for extended periods. As a result, lower concentrations of working ingredient are utilized.

Punto, L. presented an invention related to products for topical application, more particularly to improved stable emulsions for containing water soluble active ingredients, such as vitamin C, glycolic acid, etc. which may be packaged with gelatin capsules and demonstrate improved stability. It includes a novel polyethylene glycol in oil emulsion that is compatible with gelatin capsules.

Imhof, A. *et al.* examined the stability of emulsions of oil in several non aqueous polar liquids using commercially available nonionic surfactants. Stable non-aqueous emulsions were only obtained with formamide and dimethyl sulfoxide. Hydrogen bonding, and not polarity, appears to be the important factor determining the power of a solvent. Ostwald ripening plays a much more important role in the stability. Furthermore, a larger size of the surfactant molecule protects emulsions against droplet coalescence. s

Sakthivel, T. studied the effect of various parameters such as surfactant concentration and solvophilicity of the surfactant. The surface activities of polysorbate 20, 40, 60 and 80 in formamide and critical micellar concentrations were determined. Release of the model drug dehydroepiandrosterone from dodecane in formamide emulsions was studied in distilled water, the rate of release being dependent on the volume fraction of dodecane.

Payghan, S. A. gave a conceptual idea about non-aqueous system. They explained that non-aqueous systems are well known as solvents for drugs, suspension vehicles, oleogels, soft gelatin or magnoresponsive drug delivery system. It provides reservoir vehicles for transdermal systems and controlled drug delivery systems or hydrolytically unstable drugs.

Lin, C. C. studied that water increased the decomposition of deoxyArbutin in the formulations and that the polyol-in-silicone, oil-based, anhydrous emulsion system provided a relatively stable surrounding for the deoxyArbutin that delayed its degradation at 25 °C and 45 °C. Moreover, the composition of the inner hydrophilic phase, containing different amounts of glycerin and propylene glycol, affected the stability of deoxyArbutin.

There are few reports in the literature on formulation of non-aqueous emulsion. After the study of two non aqueous (oil phases) or polar solvent-oil phases it can be concluded that, there are no guidelines for stabilization of two immiscible non polar oils or polar solvent-oil phases, because HLB systems do not hold this systems. Thus there are some challenges in producing stable non-aqueous emulsions, which might be useful in formulating base for soft gelatin or magnoresponsive drug delivery system or hydrolytically unstable drugs or to provide reservoir vehicles for transdermal systems and controlled drug delivery systems<sup>19, 28</sup>. The selection of solvents for formulating nonaqueous emulsion is of importance. The development of a theoretical basis for the selection of the solvent and predicting their respective miscibility and behaviour of a surfactant is required<sup>29,30</sup>. The selection of the two phases depends largely on the polarity of the solvents. Stable oil in formamide and oil in polyethylene glycol emulsions could be prepared using commercially available non-ionic surfactants. However, it is relatively difficult to predict the applicability of other polar liquids to serve as the continuous phase. It is still unclear which combination of molecular properties can be used to predict with any certainty a stable system formed with a given surfactant, never the less, hydrogen bonding appears to play a pivotal role in determining the stability. However, formamide is closest to water in

terms of hydrogen bonding and dielectric constant and was chosen as the external phase<sup>31</sup>.

Two basic strategies could be considered when searching for stable non-aqueous micro emulsions.

(a)One is to design surfactants having two incompatible blocks, each of which is selectively soluble in either of the immiscible liquids. For example, diblock copolymers of polystyrene and polyisoprene were able to stabilise DMF and hexane emulsions for almost 24 h<sup>31,32</sup>.

(b)The other approach is to search for a suitable oil-immiscible polar liquid that can substantially replace water using existing surfactants. For example Non-ionic surfactants with HLB numbers around 12 were found to stabilize oils dispersed in formamide<sup>31,32</sup>.

The first approach has, of course, the drawback of necessitating the specific design and characterization of a new surfactant for each combination of liquids<sup>5,6</sup>. A liquid capable of replacing water in an emulsion should have an appreciable polarity to make it immiscible with oils and to make it a good solvent for the solvophilic part of the surfactant molecules. In each nonaqueous surfactant system the concept of hydrophilicity should be replaced by solvophilicity, thus defining a new scale, which incorporates interactions specific to that solvent.<sup>31,32</sup>

#### **Requirments of Non-Aqueous Emulsion:**

##### ***Non-aqueous polar solvent:***

While the term non-aqueous polar solvent is intended to include solvents generally, when the microemulsions are intended for personal care application, then the non-aqueous polar solvent should be one recognized as being pharmaceutically acceptable. In a preferred embodiment, polar liquid that exhibits a dipole moment of from 0.9 to 4.5 should be selected. Representative of some pharmaceutically acceptable non-aqueous polar solvents, which can be used, for example, in a highly preferred embodiment polar hydroxylic liquids for example, one or more of alcohols, glycols, polyhydric alcohols polymeric glycols and mixtures thereof. Preferably, the polar liquid contains an monohydroxy alcohol, such as ethanol, propyl alcohol and iso-propyl alcohol, a diols and triols , such as propylene glycol, dipropylene glycol, tripropylene glycol, butylene glycol, iso-butylene glycol, 2- and methyl-3-propane diol, a polyhydric alcohol, such as glycerin erythritol and sorbitol, or a polymeric glycol, such as polyethylene glycol, polypropylene glycol mono alkyl ethers and polyoxyalkylene copolymers. In a highly preferred embodiment, the polar liquid is selected from ethanol, propyl alcohol, iso-propyl alcohol, propylene glycol, dipropylene glycol, tripropylene glycol, butylene glycol, iso-butylene glycol, 2-methyl-3-propane diol, glycerin, erythritol sorbitol, polyethylene glycol, polypropylene glycol mono alkyl

ethers, polyoxyalkylene copolymers, glycerol esters such as glyceryl triacetate (triacetin), glyceryltripropionate (tripropionin), and glyceryltributyrate (tributytrin) etc.<sup>19,20</sup>

**Oil phase:**

(i) Volatile polydimethylsiloxanes such as hexamethyldisiloxane, octamethyltrisiloxane, and decamethylcyclopentasiloxane,

(ii) Medium Chain Triglycerides, Fatty Ester (Ethyl palmitate) etc.

(iii) Non volatile polydimethyl siloxanes having a viscosity generally in the range of about 5 to about 1,000 centistokes (mm<sup>2</sup>/s), and (i) fragrances such as musk and myrrh.

(iv) Organic oils such as natural oils derived from animal, vegetable, or mineral sources, are also suitable. Modern cosmetic oils, for example, are most representative, and among common organic oils known to be safe for cosmetic purposes are almond oil, apricot kernel oil, avocado oil, cacao butter (theobroma oil), carrot seed oil, castor oil, citrus seed oil, coconut oil, corn oil, cottonseed oil, cucumber oil, egg oil, jojoba oil, lanolin oil, linseed oil, mineral oil, mink oil, olive oil, palm kernel oil, peach kernel oil, peanut oil, rapeseed oil, safflower oil, sesame oil, shark liver oil, soybean oil, sunflower seed oil, sweet almond oil, tallow (beef) oil, tallow (mutton) oil, turtle oil, vegetable oil, whale oil, and wheat germ oil.<sup>9, 19,20</sup>

**Surfactant:**

In a preferred embodiment, the emulsion comprises one or more emulsifying agents. A range of industrial surfactants were screened using subjective visual assessment for their ability to form non-aqueous systems with medium-chain and long-chain triglycerides. The most efficient systems were formed by surfactants with predominantly unsaturated acyl chains, silicone-containing emulsifying agents, emulsifying agents derived from sorbitan compounds and emulsifying agents derived from fatty alcohols and polymeric emulsifiers. Amongst these the most efficient were oleates with HLB values of approximately 11. Sorbitan esters or ethoxylated triglycerides (e.g. Tagat TO) were usually more efficient than fatty acid ethoxylates, probably because the latter are more polydisperse since they usually contain mono and diesters.

**Role of physical properties in development non aqueous micro emulsion phases**

**(a) Critical micelle concentration-**

When surfactant are added to low concentration, the molecule exist as monomer. As the concentration of amphiphiles is increased, aggregation of monomer occur over a narrow range of concentration. Below cmc, surface active agent are preferentially adsorbed mainly at air water interface as monomer. When

surfactant monomer encounter the aqueous environment, water molecule reject the water insoluble hydrocarbon tail of amphiphiles. so tail direct away from water, while the hydrophilic head is attracted by polar water molecule by electrostatic attraction forces. As the concentration increases, the interface and the bulk phase become saturated with monomer.

**(b) particle size**

As the globule size is reduced, they tend to exhibit Brownian movement. According to diameter of globule is consider as a major factor in creaming of microemulsion. In general the rate of creaming decrease four fold, when the globule diameter is halved. In microemulsion the rate of creaming is insignificant, It is necessary to choose the optimum globule size for maximum stability.

**(c) Viscosity**

As the viscosity increases, flocculation of globule will be reduced because the mobility of globule is restricted. Simultaneously the Brownian movement of globule will also be hindered, leading to creaming. Due to this antagonistic effect, an optimum viscosity is desirable for good stability.

**(d) Physical properties of interface**

The interfacial film of the emulsifier is responsible for enhancing the stability of the product. The film should be elastic enough to form rapidly as soon as droplet are produced, This behaviour facilitates the production of micro emulsion. Suitable emulsifying agent such as surfactant should be selected to achieve the film properties at the interface. The physical properties of interface depend on the PH of the preparation. Therefore, optimum PH has to be maintained for maximum stability.

**Application:**

**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 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-surfactant. 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. 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. Microemulsions can also be used as intravenous delivery systems for

the fat soluble vitamins and lipids in parenteral nutrition.

#### **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. 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. Corneal bioavailability low due to this problem 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.

#### **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.

#### **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 antitumor antibiotic aclacinomycin A (ACM) [26]. Their findings suggested that a folate-linked microemulsion is feasible for tumor 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 tumor 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. Vyaset *al.* prepared Mucoadhesive microemulsion for an antiepileptic drug clonazepam.

#### **Other application**

##### **Magnetic Systems:**

Incorporation of magnetite nanoparticles into the disperse phase of these oil-in-oil emulsions has allowed control of the flow of droplets of the phase in capillaries, important in microfluidic systems and also in the design of pulsatile drug release systems.<sup>7, 10,22,38</sup> Magneto- and electrorheological systems are of increasing interest in controlling the properties of delivery devices.

##### **Controlled Release Vehicle:**

Non-aqueous emulsions have potential as vehicles for lipophilic drugs and potential for controlled delivery.<sup>3</sup>H-DHEA, a highly lipophilic molecule, was added to the internal phase of the emulsion and the radioactivity released in the dialysing medium of distilled water was measured. The release was observed to follow first-order release kinetics<sup>23</sup>. Certain literature showed stable anhydrous emulsions of castor oil and silicone oil. The significant factor in the stabilization of the emulsion was the solubility of the surfactants in the continuous phase, lowering of interfacial tension being not in itself sufficient. As there are no guidelines for the selection of surfactants to stabilize two immiscible non-polar oils still study is

continuing for a wider range of non-aqueous systems to develop a better understanding of stabilization. Perhaps an analogue of HLB, a lipophile (1)-lipophile (2) balance (L1L2B) may be used to predict surfactant choice<sup>23</sup>.

##### **Capsules:**

The delivery of poorly water-soluble drugs has been the subject of much research, as approximately 40% of new chemical entities are hydrophobic in nature. One area in which published literature is lacking is the field of non-aqueous emulsions filled into capsules, still some researchers have used polyethylene glycol (PEG) as a continuous phase for such emulsions<sup>1,2,3</sup> The nature of this emulsion will allow capsule filling at a later stage and it can be filled into hard gelatin as well as soft gelatin capsules. It has been suggested that these liquid systems can be administered in gelatin capsules and subsequently result in the formation of a fine emulsion within the gastric space. This process may favourably influence the Bioavailability of lipophilic drugs or help to avoid the irritancy which can be caused by high concentration of certain drugs<sup>2</sup>. Non-aqueous emulsion is inert to the capsule shells and did not compromise the seal of these systems over an extended period of time<sup>11, 26</sup>.

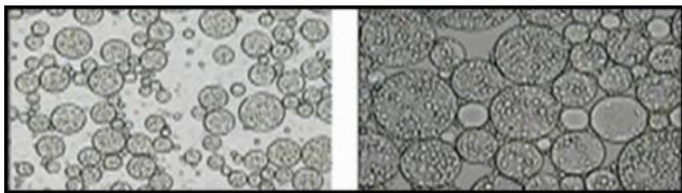
##### **Cosmetic Preparations:**

While emulsions and multiple emulsions according to the present invention are useful in any application, which can benefit from the attributes of an organosilicon material, they are primarily intended for use in personal care. Thus, they can be used alone or combined with cosmetic ingredients to form a number of over-the-counter (OTC) personal care products. For example, they are useful as carriers in antiperspirants and deodorants. They are lubricious and can improve the properties of skin creams, skin care lotions, moisturizers, facial treatments such as acne or wrinkle removers, personal and facial cleansers, bath oils, perfumes, colognes, sachets, sunscreens, pre-shave and after-shave lotions, liquid soaps, shaving soaps, and shaving lathers. They can be used in hair shampoos, hair conditioners, hair sprays, mousses, permanents, depilatories, and cuticle coats, to enhance gloss, and provide conditioning benefits.<sup>9,28,29</sup> The emulsions and multiple emulsions can function as leveling and spreading agents for pigments in make-ups, colour cosmetics, foundations, blushes, lipsticks, lip balms, eyeliners, mascaras, oil removers, colour cosmetic removers, and powders. When incorporated into sticks, gels, lotions, aerosols, and roll-ons, the emulsions and multiple emulsions can impart a dry and silky-smooth feel<sup>9,18,29</sup>.

##### **Multiple Systems:**

Having formed oil-in-oil systems and polar solvent-oil systems, it follows that multiple systems can also be

formulated. Either p.s/o/p.s or o/p.s/o for polar solvent –oil system and o<sub>1</sub>/o<sub>2</sub>/o<sub>1</sub> systems or o<sub>1</sub>/o<sub>2</sub>/w for oil in oil system formulations are possible, examples of both are shown in Figure 5<sup>22,28,29</sup>



**Figure 1:** Photomicrographs of two multiple emulsions (a) is a non aqueous emulsion, an o/o/o emulsion and (b) is an o/o/w emulsion.(a) is a formulation of castor oil-in-silicone oil-castor oil. (b) is a multiple emulsion of castor oil-in-silicone oil-in water

### Current and future development:

Formulation of non aqueous microemulsion maintain their stability and incorporate this non aqueous microemulsion successfully in topical delivery and cosmetics or personal care products.

### Conclusion:

This review gives a conceptual idea about non-aqueous system, still a challenge remains to take the formulation There is no specific stability guidelines for nonaqueous microemulsion and HLB system does not held tis system, so this was challenge for to developing non aqueous microemulsion and maintain it's stability. Well-stabilized systems will, we predict, find uses in controlled release. We are about to begin studies on formulation, drug release from intramuscular and subcutaneous depots of these non-aqueous systems.

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