

## Formulation and Characterization of Microemulsion based Gel of Antifungal Drug

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### ABSTRACT

Micro emulsion based Gel formulation provides better application property and stability & makes it dual control release system in comparison to cream and ointment. Topical Microemulsion based gel drug administration is a localized drug delivery system anywhere in the body through ophthalmic, rectal, vaginal and skin as topical routes. Many advantages of gels a major limitation is in the delivery of hydrophobic drugs. So to overcome this limitation, Microemulsion based approach is being used so that even a hydrophobic therapeutic moiety can enjoy the unique properties of gels. Whenever, it is used for fungal disease for topical delivery system so it is good for compare to oral delivery. When gels and Micro emulsions are used in combined form the dosage form are referred as Microemulsion based gel. Skin is one of the most extensive and readily accessible organs on human body for topical administration and is main route of topical drug delivery system. It is prepared by mixing an oil-in-water type or water-in-oil type emulsion with a gelling agent. The use of Micro emulsion based gels can be extended in analgesics and antifungal drugs.

**Keywords:** Co-surfactant, Gelling agent, Hydrophobic drugs, Microemulsion gel, Topical drug delivery

### INTRODUCTION

Topical delivery is used for many types of category via skin like as i.e. Antifungals, Non-steroidal, anti-inflammatory drug, Antiviral, Anti acne, etc. Human skin is well-organized membrane. i.e. Stratum corneum, the outermost layer of epidermis is formed by dead and keratinized cells. And it is an excellent barrier to penetration of drugs through the skin.<sup>[1]</sup>

#### Introduction of Topical Drug Delivery System

Topical delivery administration is a localized drug delivery system anywhere in the body through ophthalmic, rectal, vaginal, and skin as topical routes. Efforts to cure diseases have been leading in the discovery of various drugs,

medicine and delivery systems. Route of administration depends on type and severity of disease. For skin disorders topical route is most preferred. Topical drug delivery system can be defined as direct application of formulation containing medication to the skin to get localized effect of drug.

Topical drug delivery system has several advantageous such as ability to deliver drug more selectivity to specific site. Most and favourable reason for using topical delivery is avoidance of gastro-intestinal incompatibility and metabolic degradation associate with oral administration. Moreover, topical delivery provides an increased bio-availability by avoiding first pass metabolism by liver and a consistent delivery for extended period. The

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release rates of drugs from topical preparation depend directly on the physiochemical properties of the carrier and the drug employed.<sup>[2]</sup>

Gel is semisolid system of at least two interpenetrating phases: a gelling agent and a liquid. When gel and microemulsion are used in combined form and the dosage forms are referred as microemulsion based gel. Microemulsion based gels have emerged as one of the most interesting topical drug delivery system as it has dual control release system i.e gel and microemulsion. The microemulsion based gel for dermatological use has several favourable properties such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, non staining, water-soluble, longer shelf life, bio- friendly, transport, and pleasing appearance, transparent, etc. Microemulsions have gained a great attention for delivery of hydrophobic agents for systemic and local treatment. Also, gels are a relatively newer class of dosage form created by entrapment of large amounts of aqueous or hydro alcoholic liquid in a network of colloidal solid particles. Which may be consist of inorganic substances such as aluminum salts, organic polymers of natural and synthetic origin.<sup>[3]</sup>

In recent years, there has been great interest in the use of novel polymers with complex functions as emulsifiers and thickness because the gelling capacity of three compounds allows the formulation of stable microemulsions and opposite creams are decreasing surface and interfacial tension and at the same increasing the viscosity of the aqueous the water phase converts a classical microemulsion into an microemulsion based gel.

For topical delivery semisolid preparation are widely accepted over solid and liquid dosage forms. Microemulsions, which are optically isotropic and thermodynamically stable systems of water, oil, surfactant, and co-surfactant, can be used as drug delivery system because of their capacity to solubilise poorly water-soluble

drugs as well as their enhancement of topical. For topical delivery microemulsion is incorporated in to gel base to prolong the local contact to the skin.<sup>[4]</sup>

#### **Advantages of Topical Drug Delivery System.**<sup>[5,6]</sup>

- Avoidance of first pass metabolism.
- Avoidance of gastrointestinal incompatibility.
- More selective to a specific site (local action).
- Ketoconazole microemulsion based gel directly penetrate in to specific site where it suffering from fungal disease and start to results in inhibition of ergosterol synthesis.
- Suitability of drug with short half life and potent drug.
- Suitability also for self medication. Ability to easily terminate medication when needed narrow therapeutic window.
- Most and potent advantageous is that type microemulsion gel has shown low particle size so it can be easily to absorb drug through skin also permeability have be shown high.
- Improve patient compliance.
- Higher dose can be acceptable for topical drug delivery system

#### **Disadvantages of Topical Drug Delivery System.**<sup>[7]</sup>

- Skin irritation of dermatitis may occur due to the drug or excipients.
- Possibility of allergic reactions.
- Main limitations of microemulsion based gel that remains are poor absorption of microparticle via skin and entrapment of bubble during formulation.
- Some drugs of larger particle size not easy to absorb through the skin.
- Poor permeability of some drugs through skin.

#### **Transport Drug Through The Skin.**<sup>[8-11]</sup>

The epidermis is the most superficial layer of the skin and is composed of stratified keratinised squamous epithelium which varies

in thickness in different parts of the body. It is thickest on with elastic fibres. The skin forms a relatively waterproof layer that protects the deeper and more delicate structures. The outer most epidermis layer is approximately 100-150- $\mu$ m thick. And has no blood flow and induces a layer within it known as the stratum corneum. Beneath the epidermis, the dermis contains the system of capillaries that transport blood throughout the body. If the drug is able to penetrate the stratum corneum, then it can enter the blood stream and the process is known as **passive diffusion**. In the most exposed areas of the body: the hands, feet, and ears blood is also supplied to the plexus directly from the small arteries through highly muscular arteriolar venous anastomoses. Such as fatty-acids. surfactants, co-surfactants. Include enhancing solubility. Partitioning the stratum corneum, fluidizing the crystalline structure of the stratum corneum and causing dissolution of the stratum corneum lipids can enhance drug flux. The enhancement effects required to ensure delivery of pharmacologically effective concentrations are likely to be beyond the capability of chemical enhancers tolerated by the skin. Therefore, several new active transport technologies have been developed for the transdermal delivery of troublesome drugs. There are three primary mechanisms of topical drug absorption: trans-cellular, intercellular, and follicular. Most drugs pass through the torturous path around corneocytes and through the lipid bilayer to viable layers of the skin. The next most common route of delivery is via the pilosebaceous route. The barriers resides in the outermost layer of the epidermis, the stratum corneum, as evidenced by approximately equal rates of penetration of chemical through isolated stratum corneum or whole skin. Creams and gels that are rubbed in to the skin have been used for deliver pain medication and infection fighting drugs to an affected site of the body. These include, among others, gels and creams for vaginal yeast infections, topical

creams for skin infections and creams to arthritis pain.

#### **Routes of Administration.**<sup>[12]</sup>

Topical delivery generally means direct application of drug onto the skin to the site of action to get the desired pharmacological response but it has some of its own limitations such that the applied drug has to cross the different barriers of skin to reach systemic circulation such as rectal, nasal, vaginal, they have been investigated. Direct application of drug to mucus membrane led to increase in the rate and extent of absorption of drug from delivery system thus increasing its efficacy. microemulsion based gels have been investigated for various routes of administration such as buccal, vaginal, topical, etc.

### **FACTORS AFFECTING TOPICAL ABSORPTION OF DRUG**

#### **Physiological Factors**

1. Skin thickness.
2. Lipid content.
3. Density of their follicles.
4. Density of sweat glands.
5. Skin pH.
6. Blood flow.
7. Hydration of skin.
8. Inflammation of skin.

#### **Physiochemical Factors**

1. Partition coefficient.
2. Molecular weight (<600Dalton).
3. Degree of ionization (only unionized drugs gets absorbed well).
4. Effect of vehicles.

#### **Factors to be Considered When Selecting a Topical Preparation**

1. Effect of the vehicle e.g. An occlusive vehicle enhances penetration of the active ingredient and improves efficacy. The vehicle itself may have a cooling, drying, emollient or protective

action.

2. Match the type of preparation with the site (e.g., gels or lotion for hairy areas).
3. Match the type of the preparation with the type of lesions. For example, avoid greasy ointments for acute weepy dermatitis.
4. Irritation or sensitization potential. Generally ointments and w/o creams are less irritating while gels are irritating. Ointments do not contain preservatives or emulsifiers if allergy to these agents is concern.

#### Method to Enhance Drug Penetration and Absorption.<sup>[13]</sup>

1. Chemical enhancement
2. Physical enhancement
3. Biochemical enhancement
4. Supersaturation enhancement

#### Introduction of Microemulsion Based Gel.<sup>[14]</sup>

Microemulsion was first introduced by hoar and schulman in 1943. Microemulsion based gel has been increased interest during recent years in the use of topical vehicle systems that could modify drug permeation through the skin. One of the most promising techniques for enhancement of transdermal permeation of drugs is microemulsion. Microemulsions are thermodynamically stable transparent (translucent) dispersions of oil and water stabilized by an interfacial film of surfactant and co-surfactant molecules having a droplet size of less than 100nm. Microemulsions have improved transdermal permeation of many drugs over the conventional topical formulations such as emulsions and gels. Delivery of drugs using these microemulsions through skin increases the local/systemic delivery of the drug by different mechanisms that make them suitable vehicles for the delivery of antifungals.

#### Advantages of Using Microemulsion Based Gel as Topical Drug Delivery System.<sup>[15]</sup>

1. Hydrophobic drugs can be easily incorporated by using as (o/w) microemulsion in to gels: Most of the hydrophobic drugs cannot be incorporated directly into the gel base because solubility act as a barrier and problem arises during the release of the drug. microemulsion based gel helps in the incorporation of hydrophobic drugs into the oil phase and then oily globules are dispersed in aqueous phase resulting in (o/w) microemulsion. and this microemulsion can be mixed into gel base. This may be proving better stability and release of drug than simply incorporating drugs into gel base.

2. **Better Stability:** microemulsion based gel preparations are stable than other topical preparations. Like powders are hygroscopic, creams shows phase inversion or breaking and ointment shows rancidity due to oily base.

3. **Better loading capacity:** Other novel approaches like niosomes and liposomes are of nano size and due to vesicular structures may result in leakage and result in lesser entrapment efficiency. But gels due to vast network have comparatively better loading capacity.

4. **Production feasibility and low production cost:** Preparation of microemulsion based gels comprises of simpler and short steps which increases the feasibility of the production. There are no specialized instruments needed for the production of microemulsion based gels. Moreover materials are used easily available and cheaper. Hence, decreases the production cost of microemulsion based gels.

5. **No intensive sonication:** Production of vesicular molecules need to intensive sonication which may result in drug degradation and leakage. But this problem is not seen during the production of microemulsion based gels as no sonication is needed.

6. **Controlled release:** Microemulsion based gels can be used to prolong the effect of drugs having shorter half life.

### Formulation aspects of MBG for Topical Drug Delivery System.<sup>[16,17]</sup>

Formulation of TDDS mainly depends on the nature of Gelling agent, Surfactant, co-surfactant, Penetration enhancers and their concentration and temperature. In addition; factors affecting Topical absorption of the drug compound from TDDS include gelling agent concentration, co-surfactant, and oil/surfactant ratio.

**Aqueous material:** This forms the aqueous phase of the emulsion. Commonly used agents are water, alcohols. Etc.

**Oils:** Oils are the essential excipients for the TDDS. Microemulsion Based gels are microemulsion which are gelled by mixing with a gelling agent and microemulsion may be o/w or w/o type depending on the purpose of use. For pharmaceutical & cosmetic products, the oil phase until it is an active ingredient may include a wide variety of lipid of natural or synthetic origin. The consistency of these lipids may range from mobile liquids to high solids. Different oil used for formulation differs in application, properties, and utility. Like as, a number of natural oils, resulting primarily from plant sources, processed to remove impurities or to separate various fractions of the original product, are available and suitable for use in encapsulated oral formulation. Naturally occurring oils and fats are mixture of triglycerides, which contains fatty acids of varying chain lengths and degrees of unsaturation. The melting point of particular oil is directly proportional to degree of unsaturation, which also increases the relative susceptibility to oxidation. These might be hydrogenated synthetically to decrease the degree of unsaturation and conferring resistance to oxidative degradation. Both long-chain triglyceride and medium-chain triglyceride oils with different degrees of saturation have been used for the formulation

of TDDS. Modified or hydrolyzed vegetable or edible oils have contributed widely to the success of TDDS owing to their formulation and physiological advantages. Several semi synthetic liquid and thermo softening (semisolid) excipients, usually prepared by chemically combining medium chain saturated fatty acids or glycerides from natural oils are also used in topical formulations.

**Surfactants (Emulsifiers):** Surfactant molecules consist of two part, polar head group region and non-polar head group region. They are classified into four categories according to the nature of hydrophilic group within the molecule: **Anionic surfactant, Cationic surfactant, Non-ionic surfactant, Ampholytic surfactant.** Surfactant reduces the interfacial tension between two immiscible liquids and makes them miscible. When surfactants are incorporated in oil and water mixture then their polar heads is self-associated towards water phase and non-polar tails towards oil phase or they can easily locate at the interface, which is thermodynamically very stable. Non- ionic surfactants with a relatively high hydrophilic-lipophilic balance (HLB) were used for the design of topical drug delivery systems, where the various liquid or solid polyoxyethylene 20oleate (Tween 80) are the most frequently used excipients. Emulsifiers derived from natural sources are expected to be safer than synthetic ones and are recommended for TDDS (topical drug delivery system) use despite their limited ability to emulsification. Non-ionic surfactants are known to be less toxic compared to ionic surface-active agents. Also, they may cause moderate reversible changes in cell membrane. The high HLB and subsequent hydrophilicity of surfactants is necessary for the immediate formation of o/w droplets and rapid spreading of the formulation in the aqueous environment. Surfactants being amphiphilic in nature are capable of dissolving relatively high quantity of lipophilic drug compound. This

prevents precipitations of the drug in lipid barrier and facilitates greater absorption. A cationic emulsion has greater bioavailability than an anionic emulsion. The self-emulsifying lipid formulations are of two kinds namely, Emulsion based gel for Topical Drug Delivery Systems formed using surfactants of HLB < 12 and Microemulsion based gel for Topical Drug Delivery Systems formed with surfactants of HLB > 12. Concentration range for preparation of stable microemulsion based gel for topical drug delivery system lie b/w 30 to 60%.

**Co-surfactants (Co-emulsifiers):** Relatively high concentration (usually, more than 30%w/w) are needed in order to produce an effective microemulsion for topically drug delivery system. Organic solvents: which is Suitable for topical administration (ethanol, propylene glycol (PG), polyethylene glycol (PEG), etc) may help to dissolve large amounts of either the hydrophilic surfactant or the drug in the lipid base. These solvents sometimes play important role of the co-surfactant in the microemulsion systems. Polymeric liquid and semi-solid excipients can be used alone or in mixture with other lipid excipients to improve solubilizing power of formulation. Among the polymeric glycol based excipients, PEGs are versatile, well characterized and widely applied class of solubilizers which are available as both liquid and thermo softening semisolid.

**Gelling agents:** Addition of gelling agent to these formulations gives a gelled structure. Gelling agent are of two types: natural and synthetic. Incorporation of gelling to a system makes it thixotropic. According to the Swedish national encyclopedia: thixotropy is “property of viscous (viscid) or gel-like product turning more liquid as the longer time and the more vigorous, which is deformed (i.e stirring).” It is generally accepted thixotropy the phenomenon of the fluid which shows a reversible structural. Carbopol polymers are polymers of acrylic acid cross-linked with polyalkenyl ethers or divinyl glycol. They are produced from primary polymer particles of less a diameter. Each particle can be viewed as a network structure of polymers chains interconnected via cross-linking. Carbomers readily absorb water and get hydrated and swell. Besides it's hydrophilic in nature, its cross-linked structure and it's insolubility in water makes carbopol a potential candidate for use in controlled release drug delivery system. Effect of gelling agent has been studied on release rate of drug from microemulsion based gel. It has been found. That is an inverse correlation b/w the concentration of gelling agent and the extent of drug released. Others type including synthetic, semi-synthetic, natural gelling agent can also be employed.

**Table 1:** Various gelling agent used for formulation of Emulgel & MBG

Gelling agent	Advantages	Concentration (%w/w)	Dosage form
Carbopol-934	Form gels at very low concentration & provide control release of incorporated drug	1%, 1.78%	Emulgel, MBG
Carbopol- 940	Form highly viscous gels and provide controlled release of incorporated drug	1%	Emulgel, MBG
HPMC-2910	Produce neutral gels of very stable viscosity. Microbial resistance & good film strength.	2.5%, 5%	Emulgel
HPMC	It showed better drug release rate	3.5%	Gel
NaCMC	Suitable for sterile gels as it can stand autoclaving without serious deterioration	3-4%	Gel



**Penetration Enhancers:** Penetration enhancers are the agents which increases the penetration power of the drug through skin. In order to promote absorption of drugs through skin barrier, vehicles often include penetration enhancing ingredients which temporarily disrupts the highly ordered structure of stratum corneum skin barrier, fluidize the lipid channels between corneocytes, alter the partitioning of the drug into skin structures, or otherwise enhance delivery into skin.

**Table 2: List of Penetration Enhancers**

Penetration Enhancer	Concentration used (%w/w)	Dosage form
Oleic acid	1%	Emulgel
Lecithine	5%	Gel
Urea	10%	Gel
Isopropyl myristate	5%	Gel
Linoleic acid	5%	Gel
Clove oil	8%	Emulgel
Menthol	5%	Emulgel

#### EVALUATION OF MICROEMULSION. <sup>[18-20]</sup>

**Droplet size measurements:** Size analysis of microemulsion is carried out by dynamic light scattering with zetasizer (Malvern instruments Ltd., Malvern, U.K). polydispersity index of the formulation was determined by the same instrument.

**Zeta potential measurements:** This is used to identify the change of the droplets. In conventional emulsions, the charge on an oil droplet is negative due to presence of free fatty acids. Zeta potential for microemulsion is determined using zetasizer (Malvern instrument Ltd. UK).

**Conductivity measurement:** the measurement of electrical conductivity gives the quantitative idea of the solubilization of water phase in the selected mature containing oil phase, surfactant and co-surfactant. It also gives the idea about the types of microemulsion. The oil, surfactant, and co-surfactant concentration is selected as per optimized formulation. Then the water phase is added drop wise to the mixture of the oil and amphiphiles and electrical conductivity

of formulated is measured using a conductometer at ambient temperature.

**Transmission electron microscopy:** Oil globules of microemulsion were visualized using TEM, Philips Technai-20 electron microscope (Philips, Holland) with an accelerated voltage of 20-200 kv. The samples were negatively stained with a 1% aqueous solution of phosphotungstic acid (PTA). Microemulsion was dried on a carbon coated copper grid. After drying, the samples were viewed under microscope 80 kv.

#### Evaluation of Microemulsion Based Gel. <sup>[21-22]</sup>

**Physical appearance:** the prepared gellified microemulsion formulations were inspected for their color, homogeneity, consistency and pH. The pH values of 1% aqueous solutions of the prepared Gellified microemulsion is measured by a pH meter.

**Spreadability measurement:** to determine the spreadability of microemulsion based gel, 0.5 g of gel was placed within a circle of 1 cm diameter pre-marked on a glass plate, over which a second glass plate was placed. A weight of 500g was allowed to rest on the upper glass

plate for 5min. The increase in the diameter due to gel spreading was noted.

**Rheological study:** The viscosity of microemulsion based gel formulation was determined at 37°C using a brook field viscometer (Brookfield DV-E viscometer). 62 number spindle was set at 12 rpm.

**Drug content determination:** Take 1gm microemulsion based gel. Mix it in suitable solvent. Filter it to obtain clear solution. Determine its absorbance using UV spectrophotometer. Standard plot of drug is prepared in same solvent. Concentration and drug content can be determined by using the same standard plot by putting the value of absorbance.

**Extrudability (Tube test):** It is usual empirical test to measure the force required to extrude the material from tube. The method adopted for evaluating microemulsion based gel formulation for extrudability. And it is based upon the quantity in percentage of gel and gel extruded from aluminium collapsible tube on application of weight in grams required to extrude at least 0.5 cm ribbon of microemulsion based gel in 10 seconds. More quantity extruded better is extrudability. The extrudability is than calculated by using the following formula.

Extrudability = Applied weight to extrude microemulsion gel from tube (gm) / Area (cm<sup>2</sup>)

**In vitro release study/ permeation studies:** Franz diffusion cell (with effective diffusion area 3.14 cm<sup>2</sup> and 15.5 ml cell volume) was used for the drug release studies. Microemulsion based gel (1g) was applied onto the surface of cellophane membrane evenly. The cellophane membrane was clamped between the donor and the receptor chamber of diffusion cell. The receptor chamber was filled with freshly

prepared PBS (pH 7.4) solution. The samples collected at suitable time interval. Samples were analyzed for drug content by UV spectrophotometer at suitable wavelength after appropriate dilutions. The cumulative amount of drug released across the mice shaven skin was determined as a function of time.

**Antifungal activity:** Antifungal activity of formulation is checked by cup-plate method. A definite volume of the Candidia Albicans suspension (inoculum) was poured into the sterilized sabouraud dextrose agar media (cooled at 40°C) and mixed thoroughly. About 20 ml of this suspension was poured aseptically in the Petri plates and kept till the solidification. The surface of agar plates was pierced using a sterile cork borer. The prepared wells were filled with equal volume of drug containing microemulsion based gel, microemulsion based gel without drug. After incubation for 18 to 24 hours at 25°C, the fungal growth was observed and the zone of inhibition was measured using antifungal zone reader.

**Ex-vivo Bioadhesive strength measurement:** the modified method used for the measurement of bioadhesive strength. The fresh skin is cut into pieces and washed with 0.1N NaOH. Two pieces of skin were tied to the two glass slide separately from that one glass slide is fixed on the wooden piece and other piece is tied with the balance on right hand side. The right and left pans were balanced by adding extra weight on the left-hand pan. 1gm of topical microemulsion gel is placed between these two slides containing hairless skin pieces and extra weight from the left pan is removed to sandwich the two pieces of skin and some pressure is applied to remove the pressure of air. The balance is kept in this position for 5 minutes. Weight is added slowly at 200mg/min to the left-hand pan until the patch detached from the skin surface. The weight (gram force) required to detach the microemulsion gel from



the skin surface gave the measure of bioadhesive strength. The bioadhesive strength is calculated by using following formula.

Bioadhesive strength = Weight required (gms)/  
Area (cm<sup>2</sup>)

**Stability studies:** The prepared microemulsion based gel were packed in aluminium collapsible

tubes (5gm) and subjected to stability studies at 5°C, 25°C/60% RH, 30°C/65% RH, and 40°C/75% RH for a period of 3months. Samples were withdrawn at 15-day time intervals and evaluated for physical appearance, pH, rheological properties, drug content, and drug release profiles.

#### APPLICATIONS. <sup>[23]</sup>

Product Name	Drug	Manufacturer
Voltaren emulgel	Diclofenac diethyl ammonium	Novartis Pharma
Miconaz-H-emulgel	Miconazole nitrate, Hydrochloride	Medical union Pharmaceuticals
Excex gel	Clindamycin, Adapalene	Zee laboratories
Pernox gel	Benzoyl peroxide	Cosme Remedies Ltd.
Lupigyl gel	Metronidazole	Lupin Pharma
Clinagel	Clindamycin phosphate Allantoin	Stiefel Pharma
Avindo gel	Azithromycin	Cosme Pharma laboratories

Topical semisolid dosage forms are the most preferred for treat fungal infections. Ketoconazole is an imidazole antifungal drug belonging to the class-II of biopharmaceutical classification system. If we can use ketoconazole in formulation by orally so we have suffered many Problem like as oral absorption of ketoconazole often causing therapeutic failure. Weather microemulsion based gel for topical drug delivery system formulation of ketoconazole would be able to overcome the pH dependent dissolution and oral bioavailability. And also increase permeability. This drawback researches were carried out to identify the potential of various Topical drug delivery system as carrier of anti fungal agents in these semisolid dosage forms.

#### MARKETED PREPARATION OF EMULGEL & GEL

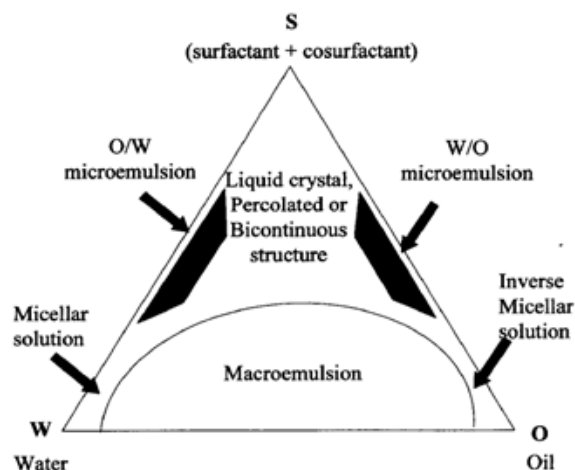
##### Method of Preparation [Microemulsion] <sup>[24,25]</sup>

##### Phase titration method.

Microemulsions are prepared by the spontaneous emulsification method (phase titration method) and can be drawn with the need of phase diagrams. Construction of phase diagram is a useful method to study the complex series of interactions that can occur when different components are mixed. Microemulsions are formed along with various association diagram (including emulsion, micelles, lamellar, hexagonal, cubic, and various gels and oily dispersions) 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 intercept. Pseudo structure is often constructed to find the different zones including microemulsion zone. In which each corner of the diagram represents 100% of the particular component **Figure**. The region can be separated into w/o or o/w microemulsion by simply considering the composition whether it is oil rich or water rich. Observations should be made carefully so that the metastable systems are not included.



**Figure.** Pseudo-ternary phase diagram of oil, water and surfactant showing microemulsion region.

#### Phase Inversion Method.

Phase inversion of micro emulsion occurs upon addition of excess of the dispersed phase or in the response in temperature. During phase inversion more changes occurs that includes change in particle size that can effect drug release in to in-vivo and in-vitro side. These methods make use of changing the spontaneous curvature of the surfactant. For non-ionic surfactant, this can be achieved by changing the temperature of the system, forcing a transition from an o/w micro emulsion at low temperature to a w/o micro emulsion at higher temperature. During cooling, the system

crosses the 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 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 micro emulsion to o/w micro emulsion at the inversion locus. Short chain surfactant from flexible monolayer at the o/w interface resulting in a bicontinuous micro emulsion at the inversion point.

#### CONCLUSIONS

In the recent years, topical drug delivery system will be used extensively due to better patient compliance. Since Microemulsion based gel possesses an edge in terms of spreadability, adhesion, also transparent microemulsion, viscosity, antifungal activity. They will become a popular drug delivery system. Moreover, they will become a solution for loading hydrophobic drugs in a water soluble gel bases.

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