



## Phytoconstituent Based Microemulgel: A Novel Topical Drug Delivery Approach

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### ABSTRACT

A huge amount of Indian medicinal plants are accredited with various pharmacological activities. Extract of medicinal plant and extracted oil have more or less pharmacological property, some natural penetration enhancers have advantages such as low cost, better safety profile hence they increase their acceptances in the formulation of microemulgel. Some of oil may assist the therapeutic action of API. It is convenient, cost-effective to use of herbal oil as oil phase or API, penetration enhancer, surfactant or other constituent in microemulgel formulation. Microemulgel is a microemulsion and gel combination with herbal ingredient, with small sized globule present in an emulsion. Microemulsion consists of delivering a drug dissolved in a mixture of one or more excipient like mono, di, and triglycerides, lipophilic and hydrophilic co surfactant. Microemulsion is formed when entropy changes in that dispersion is greater than the free energy require increasing the surface area between oil and aqueous phase of dispersion. Microemulgel has a dual action of microemulsion and gel. Emulsion based gel, the drug get entrapped in cross linkage network of gelling agent. In that small drug get entrapped and release in controlled manner. Microemulgel have other advantages like good uniformity, easily spreadable, greaseless as well as bio-friendly, detachable, non-staining, emollient, longer shelf-life, transparent, pleasant appearance, the ability of patients for self-medication, termination of medications will be easy.



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### INTRODUCTION

Recent several years, great improvements have been made on the development of novel drug delivery systems (NDDS) for plant actives and extracts. Several plant extracts and phytoconstituents having excellent bioactivity. Herbal medicines are easily available, cheaper, and safer than the synthetic drug. The variety of novel herbal formulations like polymeric nanoparticles, nanocapsules, phytosomes, microemulsion, emulgel, and microsphere has been reported using bioactive and plant extracts. Phytoconstituent based Microemulgel, is a microemulsion and gel combination with the herbal ingredient, with small-sized globule present in an emulsion. The microemulsion concept was intro-

duced in 1940 by hoar and Schulman generated a clear single-phase solution by titrating a milky emulsion with hexanol. The microemulsion is defined as thermodynamically stable, optically isotropic liquid solution which is formed by combining oil, water, and surfactant and Cosurfactants as shown in Figure 1 (Lawrence and Rees, 2012).

Microemulsion consists of delivering a drug dissolved in a mixture of one or more excipient like mono, di, and triglycerides, lipophilic and hydrophilic co-surfactant. Microemulsion content more quantity of emulsifier: These emulsifiers lower the interfacial energy between the oil phase and aqueous phase. The difference between emulsion and microemulsion; emulsion is thermodynamically unstable and both phases will get separated as time passed on. In the case of the microemulsion, the presence of surfactant and cosurfactant reduces interfacial tension by formatting barrier. The microemulsion is formed when entropy changes in that dispersion are greater than the free energy require increasing the surface area between the oil and aqueous phase of dispersion. The change in free energy (G) associated with the process of emulsification ignoring the free energy of mixing can be expressed by McClements (2012).

$$\Delta G = \sum_{N_i=no. \text{ of droplet of radius } r_i} N_i \pi r_i^2 \sigma$$

$\sigma = \text{interfacial energy}$

The microemulsion is of two types of emulsion either oil in water and water in oil emulsion. In microemulsion, drug present solubilized form in small-sized droplet which provides a large surface area for absorption. Apart from these, present excipient help to improve bioavailability, lipid enhancing permeability of drug. The surfactant and co-surfactant itself act as a penetration enhancer also.

The nanosized globule of microemulsion (10 $\eta$ m - 140 $\eta$ m) use in combination with the gelling agent, these combined dosage forms are referred to as microemulgel. Nanosized emulsion using with gelling agent enhance retention time of formulation dosage form (drug moiety) and permeability. Other topical agents like ointment, cream, lotion have many disadvantages like very sticky, uneasiness to apply, lesser spreading coefficient, need to apply with rubbing and they also have problems with stability. Due to all these issues within the major group of semisolid preparations, the use of transparent gels has useful both in cosmetics and in pharmaceutical preparations. Despite many advantages of gels have a major limitation in the delivery of hydrophobic drugs; to overcome this limitation an emulsion-based approach is being used.

A hydrophobic therapeutic moiety can be successfully incorporated and delivered through a gel. The emulsion has two-phase, internal phase, and external phase. Internal phase pass drug moiety to the external phase slowly gets absorb in the skin. Emulsion based gel, the drug get entrapped in a cross-linkage network of gelling agent. In that small drug get entrapped and release in a controlled manner. The stability of emulsion also gets increases as well as increasing penetration ability. Gel matrix influence by type and concentration of polymer is used to prepare, it also affects the release rate of the drug (Phad et al., 2018).

## Formulation components

### Oil phase

The emulsion is made up of oil phase and water phase hence the selection of oil has great importance in emulgel formulation. The oil phase affects the viscosity, permeability, and stability of the formulation of emulsion. Oil has less hydrophobic property shows better emulsification. If hydrophobicity increases it gives effect on the solubility of a lipophilic drug as shown in Figure 2. Edible oil and vegetable oil show poor capability to dissolve a large amount of lipophilic drug and poor emulsification property. Hence, chemically modified oil, like medium-chain triglyceride or mono- or diglyceride is used as an oil phase for poorly water-soluble drugs. Medium-chain triglycerides are appropriate for encapsulation of drugs with log p-value ranging from 2 to 4. Recent advancements in the formulation that those oils have medicinal value, itself use as an oil phase as well as an active drug ingredient. Some oil also known for their synergistic effect, they used as a penetration enhancer improve permeability drug through the skin. Some of the oil known for its active properties like anti-inflammatory, antimicrobial, antiseptic. Various oils used as oil phase in formulation of emulgel as given in Table 1 (Jäger et al., 2008).

### Surfactant

The emulsion is a combination of two immiscible liquid, thermodynamically unstable which is stabilized by using an appropriate emulsifier. The emulsifier used to reduce the interfacial tension between the oil phase and water phase makes stable formulation by avoiding coalescence of nanodroplet emulsifier should be safe, high drug loading capacity, good emulsifying capacity along with better stability. Proper selection of emulsifiers is an important feature due to associated toxicity and a large quantity of surfactants may cause irritation to skin.

HLB values of surfactants show a greater effect on

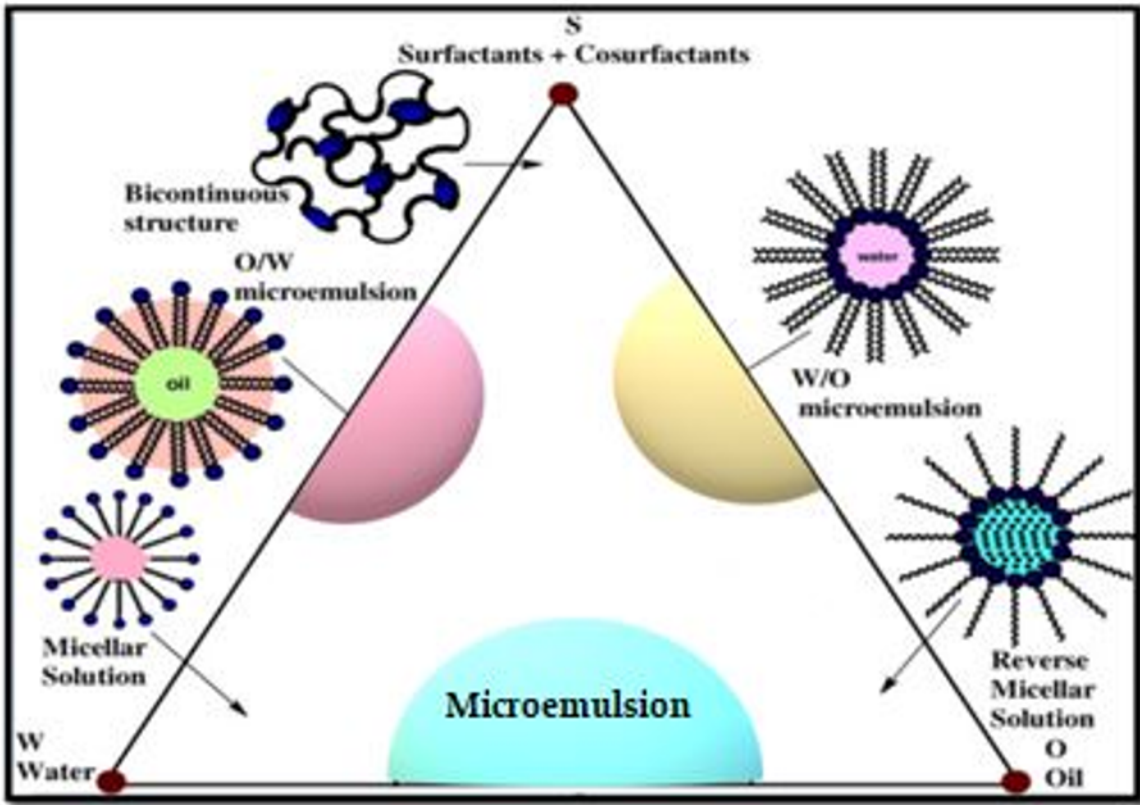


Figure 1: pseudo ternary phase diagram of microemulsion

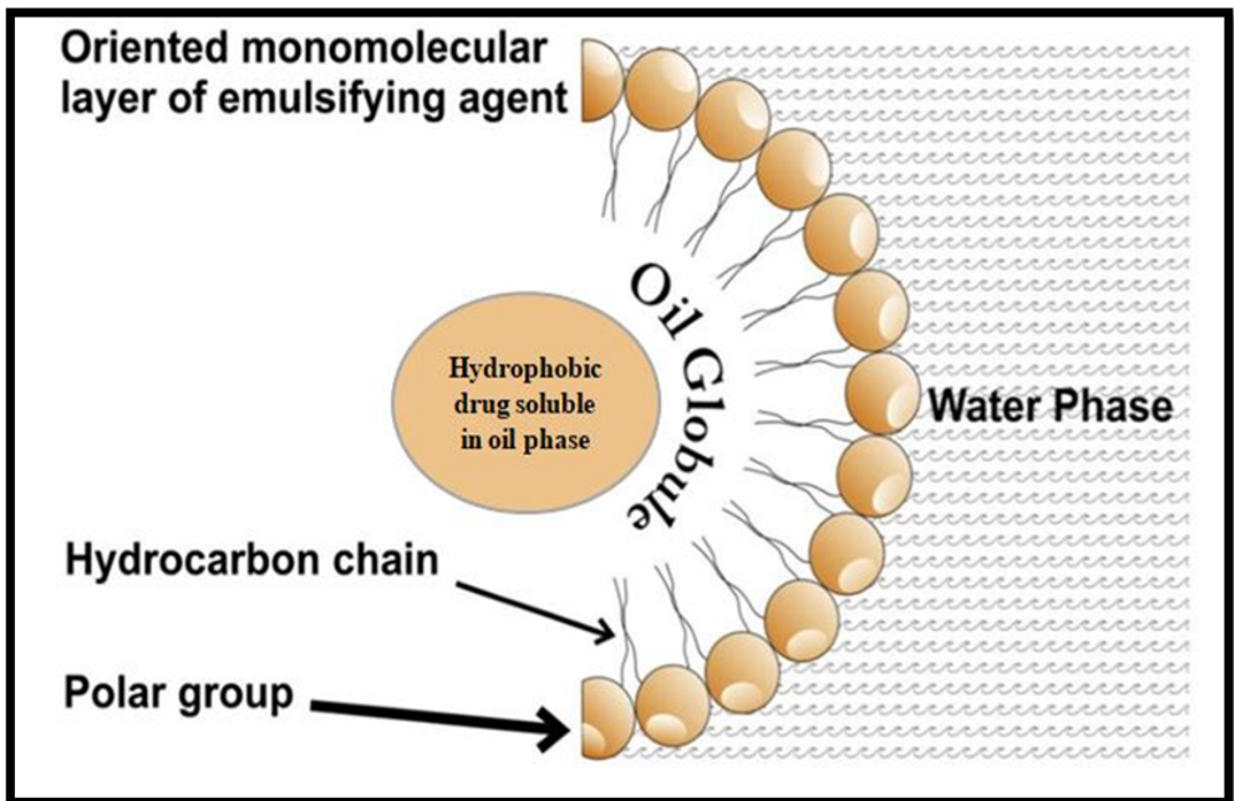


Figure 2: Dispersion of Drug Containing Oil Globule in Surfactant

**Table 1: Various Oils Used as Oil Phase in Formulation of Emulgel**

Oil name	Source	Property	Identity	Formulation prepared	Category used for combination
Myrrh oil	Commiphora myrrha	Antimicrobial, antiviral, antifungal	Vegetable oil	Ointment, microemulsion	Antifungal, antiviral (Beitz, 2005)
Rose hip oil	Rosa vegetable moschata oil	Anti bacterial	Vegetable oil	Lotion ,gel	Topical NSAID, topical steroid (Beitz, 2005)
Birch oil	Betula alba	Analgesic, antiseptic	Vegetable oil	Cream, ointment ,gel	Corticosteroid, anti-microbial (Fei et al., 2011)
Balsam oil	Myroxylon peruviatta	Anti-bacterial, anti-parasitic, anti-fungal	Vegetable oil	Gel, emulsion, ointment	Antifungal, topical antibiotics (Fei et al., 2011)
Thyme oil	Thyme plant	Anti-spasmodic, anti-rheumatic, bactericidal	Vegetable oil	Biodegradable film, cream, nanoemulsion	Topical antibiotics, topical NSAID (Jing et al., 2003)
Wheat germ oil	Wheat kernel	Anti-inflammatory & anti oxidant	Vegetable oil	Microemulsion, ointment, cream	Drug for psoriasis, NSAID, topical steroids (Jing et al., 2003)
Olive oil	Olive seeds	Moisturizer, anti-oxidant , anti cancer	Vegetable oil	Emulsion, microemulsion, cream	Anti-oxidant ,anti-microbial (Jing et al., 2003)
Castor oil	Ricinus communis	Anti-inflammatory, Anti-oxidant	Vegetable oil	Ointment, microemulsion, nanoemulsion, creams	Topical NSAID, antioxidants (Silva et al., 2015)

the formulation. If to be obtaining water in oil emulsion formulation, then the HLB value of emulsifier should be 3-8. HLB value 8-12 for oil in water emulsion formation of the stable microemulsion can be obtained by mixing low and high HLB surfactant, the hydrophilic and lipophilic emulsifier are thought to align alongside each other imparting rigidity and strength to the emulsifier film through hydrogen bonding and making microemulsion more stable. In microemulsion, the special attention given to the solubility of oil and drug, surfactant, and co-surfactant.

By adding a surfactant, similar ionic charge present on the surface, they prevent aggregation of the droplet and stabilize microemulsion. Surfactants

are divided into 3 classes depending on their ionic nature. cationic surfactant (amine and quaternary ammonium compound, acetyl trimethyl ammonium bromide, lecithin, hexcetyl trimethyl ammonium bromide , dodecyl dimethyl ammonium bromide) non-ionic surfactant capryol 90, labra filcs, labrasol, gelucire 44/14, cremophore RH40, PEG MW >4000, Poloxamer 124,188,softigen 701, tween 80, tween 60.

Anionic surfactant-containing carboxylate group, sodium bis-2-ethylhexylsulfosuccinate, sodium dodecyl sulfate, zwitterionic surfactant (phospholipid). Generally, non-ionic surfactant mostly chosen for the reason that, it gets less affected by pH and changes in ionic strength, biocompatibility,

**Table 2: Phytoconstituents with different gelling agents Used For Development of Emulgel**

Aim	Category	Drug	Gelling agent	Used phytoconstituent	Major Observation
Microsponges based Emulgel	Wound healing activity	Atorvastatin calcium	carbopol 934	emu oil as penetration enhancer	5% emu oil emulgel has excellent wound healing activity ( <a href="#">More et al., 2016</a> )
Formulation of Polyherbal Micro-emulgel	treatment of Arthritis	Tinospora cordifolia and Curcumin	carbopol 940P	Tinospora cordifolia and Curcumin	Oil globules of Micro-emulgel were in range of 1.50 to 2.13 $\mu$ m ( <a href="#">Thakur et al., 2016</a> )
Novel Jojoba Oil-Based Emulsion Gel Formulations	antimitotic activity	Clotrimazole	HPMC and Carbopol 934 P	jojoba oil	Formulation containing low level of Carbopol or combination of two gelling agents have better stability ( <a href="#">Shahin et al., 2011</a> )
Development of Sunscreen Emulgel	Sunscreen	Cinnamomum Burmannii	Carbopol 934	Cinnamomum Burmannii Stem Bark Extract	Extract and formulated emulgel have potency to protect against UV-B radiation. ( <a href="#">Priani et al., 2012</a> )
Formulation and evaluation of gel and emulgel	to relieve the pain	Chili extract (capsicum frutescence)	Carbopol-940	Olive oil	Proved that rate of penetration of emulgel capsaicinoid faster than gel. Capsaicinoid is not soluble in water. ( <a href="#">More et al., 2016</a> )

and safety. Toxicity and skin irritation issue ionic surfactant less preferred. Nowadays, natural surfactants take place because of their less toxicity, biocompatibility, biodegradability. They are amphiphilic in nature affinity for both hydrophilic and hydrophobic. It works on the same mechanism, prevent aggregation by forming repulsive force ([Liu et al., 2012](#)).

### Co-surfactant

The only surfactant cannot give transient negative interfacial tension. Co surfactant gives flexibility to the interfacial film by modifying the curvature of oil in water interface which improves oil solubilization. Cosurfactants when combined with surfactants penetrate through surfactant and disturb interfacial film and give required fluidity, provide emulsification by lowering interfacial tension. Surfactant and cosurfactant affect release by partitioning of a therapeutic agent or lipophilic drug in aqueous and oil phase.

The selection of surfactant and co-surfactant also depend upon the transmittance. Transcutol P shows a higher percentage of transmittance and penetration enhancer properties than propylene glycol and Ethanol. The ratio of surfactant and co-surfactant has a great influence on the microemulsion area in the phase diagram. Only surfactant not able to reduce surface tension sufficiently, surfactant, and co-surfactant in equal ratio greatly reduce interfacial tension, give the higher microemulsion area in the phase diagram. But the increase in surfactant in the ration (3:1) may be decreased in the area. 1, 2 propylene glycol, PEG 400, carbitol, absolute ethyl alcohol, propanol, butanol are used as a surfactant in a microemulgel, microemulsion.

Alcohol is generally used as a cosurfactant in the microemulsion. Addition cosurfactant (e.g. Ethyl alcohol) may give positive curvature effect alcohol swells head region so, it becomes more hydrophilic and formed o/w type emulsion. In the case of longer

**Table 3: Various Natural Penetration Enhancers (NPE)**

Phytoconstituent	Source	Major observation
NPE'S are new class of penetration enhancer due to its advantages such as low cost, better safety profile more research need to be focused in this field to develop a stable topical and transdermal formulations containing NPE which can be scale up for commercial drug product ( <a href="#">Shah et al., 2011</a> ).		
Papain	Papain is isolated from carica papaya	The combined administration of LMWH and Papain was a new approach in improvement in absorption
Piperine	Piperine is obtained from mature fruits of piper nigrum and piper lingam	Piperine enhances transdermal permeation of aceclofenac ( <a href="#">Shah et al., 2011</a> )
Capsaicin	Capsaicin is a major alkaloid is produced only in capsicum fruits	Capsaicin increases the penetration of naproxen through SC route.
<b>Essential oil</b>		
As penetration enhancer, essential oils help in the delivery of drug compounds into the skin by interacting with the intercellular lipids by different physical processes. They penetrated easily by the skin, they are easily excreted; due to their better safety profile they are most prepared ( <a href="#">Akbari et al., 2015</a> )		
Eucalyptus oil	Oil of Eucalyptus can be obtained from a number of species of the myrtaceae family	10% (v/v) eucalyptus oil increases the permeation of chlorhexidine than 70% (w/v) isopropyl alcohol used in formulation ( <a href="#">Karpanen et al., 2010</a> )
Niaouli oil	Extraction of Niaouli oil made by steam distillation of twigs and leaves of Melaleuca Quinquenervia	It was found that Niaouli oil more effective in transdermal permeation of estradiol
Black cumin oil	Extraction of black cumin oil is made by steam distillation of the seeds of Cuminum Cyminum	Black cumin oil showed a greater permeating effect for carvedilol ( <a href="#">Amin et al., 2008</a> )
Fennel oil	The extraction of fennel oil can be made from the seeds of Foeniculum Vulgare	Percutaneous penetration of Trazodone Hydrochloride was enhanced by fennel oil
Almond oil	Oil of almond and oleic acid	Oil of almond and oleic acid were found as promising carriers/vehicles for enhanced permeability and solubility of Aceclofenac ( <a href="#">Malik et al., 2014</a> )
Alpinia Oxyphylla oil	Oxyphylla oil was extracted from a Oxyphylla	Oxyphylla oil was having more efficient permeation enhancing the effect of indomethacin at concentration 3% and 5%

*Continued on next page*

Table 3 continued

Phytoconstituent	Source	Major observation
Basil oil	Basil oil is obtained from the Ocimum basilicum Herb	Basil oil was studied as a permeation enhancer for labetalol hydrochloride
Turpentine oil	Turpentine oil is made from the resin of certain pine trees	The permeation enhancing showed increasing permeation with increasing concentration
Rosemary oil	Rosmarinus officinalis plant	Analgesic effect of topical preparation significantly dependent on concentration containing 0.5 and 1% of rosemary essential oil (Akbari et al., 2015)
Cardamom oil (clove oil)	Cardamom (Elettaria Cardamomum) is a common spice of India belonging to the zingiberaceae family	Cardamom oil on in vitro permeation studies through the rabbit abdominal skin showed an increase in penetration of the drugs indomethacin, diclofenac, and piroxicam

### Terpenes

Terpenes are a large and diverse class of organic compounds, produced by a variety of plants, particularly conifers or by some insects. Terpene showing the effect on the skin, in particular, its lipophilicity. Smaller terpenes with nonpolar groups are said to be better skin permeation enhancers (Yi et al., 2016).

Farnesol	Farnesol is present in many essential oils, such as citronella, neroli, cyclamen, lemongrass, tuberose, balsam, and tolu	Farnesol (0.25%) was reported to increase the permeation of diclofenac sodium
Menthol	Obtained from the flowering tops of mentha piperita	Menthol and Limonene together can be used as a prototype of terpenes used as permeation enhancer
Eucalyptol	Eucalyptol is a cyclic ether and a monoterpenoid known by a number of synonyms such as 1, 8-cineole, cajepitol, eucalyptol, and cineole	1, 8-cineole has also been used for the percutaneous absorption of several lipophilic drugs
Eugenol	Especially obtain from clove oil, nutmeg, cinnamon	In vitro studies showed that eugenol does increase the permeation
Borneol	Borneol is a white colour lump-solid with a sharp camphor-like odour	Borneol effectively promoted the transdermal permeation (Yi et al., 2016)

chain cosurfactant (acetyl alcohol) swelling more, in chain region than the head region and formed w/o type microemulsion (More *et al.*, 2016).

### Gelling agent

The gelling agent is used as a thickening agent which increases the consistency of any dosage form. According to the Swedish national encyclopedia, thixotropy is a viscous or gel-like product turning more liquid vigorously for a longer period they get deformed. Generally accepted that thixotropy is the phenomenon of fluid that shows a reversible structural transition (gel- sol-gel) conversion due to time-dependent changes in viscosity induced by temperature, pH, or other components without any changes in the volume of the system. Synthetic, semisynthetic natural gelling agent present in natural gelling agent like guar gum, xanthan gum lead to microbial degradation, hence, synthetic and semisynthetic gelling agent replaces natural agent. Hydroxyl propyl methylcellulose, various grades of carbopol, sodium carboxymethyl cellulose used as a gelling agent. Hydroxyl propyl methyl cellulose is an odorless, tasteless, white to slightly off-white free flowing granular powder.

Synthetic modification of natural polymer is cellulose Carbopol is the polymer of acrylic acid cross-linked with poly alkenyl ethers, or divinyl glycols have particle size about 0.2 to 0.6  $\mu\text{m}$  in diameter. It is insoluble in water and form cross-linkage used for the controlled release of drugs. Gelling agent effect on the release rate of the drug. There is an inverse correlation between the concentration of gelling agents and the amount of drug release. It also depends upon the type of gelling agent used.

The combination of two gelling agent shows better stability, HPMC based Emulgel found to be better than carbopol based emulgel shows improved drug release rate. In this stage, the emulsion will be introduced into the prepared gel at a particular ratio, with continuous mixing to form homogeneity.

Gelling agents in microemulsion formulation is to change its physical state, from liquid to gel which also affects the pharmacokinetic properties of drugs incorporated this Nanocarrier system. Gelling agent prepared by adding gelling agent into aqueous media with continuous stirring at a constant rate at specified condition after swelling addition of emulgel into it. Details of various gelling agents used to develop emulgel of phytocostituents are given in Table 2 (Thakur *et al.*, 2016).

### Penetration enhancer

Penetration enhancers help in the permeation of the desired drug through the skin by dropping the

impermeability of the skin. These agents interact with skin constituent to induce temporary disrupt skin barrier and lipid barrier, increases skin permeability.

Some properties which are desired in permeation enhancers are the must be pharmacologically inert, non-irritating, nontoxic, no allergic, compatible with drugs and excipients, odorless, tasteless, colorless, and inexpensive and also have good solvent properties. Few Natural Penetration Enhancers (NPE) are summarised in Table 3.

### Formulation method of microemulgel

Microemulgel formulated with two steps, first is the formulation of microemulsion by using surfactant and co-surfactant with drug dissolution, followed by the second step that is the formulation of gelling agent and incorporation of microemulsion into these gelling agent.

Microemulsions are isotropic systems, which are difficult to formulate because their formulation is a highly specific process involving spontaneous interaction among constituent molecules. For the preparation of microemulsion basically two methods i.e. low energy and high energy emulsification method.

### Low energy emulsification method

Low energy method advantages over high energy methods for the formulation of the microemulsion. The low energy method includes the phase inversion method and the spontaneous method. In the phase inversion method, the mixing of oil, water, and surfactant in a predefined ratio. Constant stirring required at moderate speed with titrating of oil phase with an aqueous phase, so the formation of a nanosized droplet in a continuous phase. The addition of surfactant and co-surfactant affects the emulsification process.

Type of surfactant used determined which type of emulsion formed, the temperature is extremely important in determining the effective head group size of non-ionic surfactant. At low temperatures, they are hydrophilic and form normal oil in the water system. At higher temperatures, they are lipophilic and form water in the oil system. At an intermediate temperature, microemulsion occurs with the water and oil phase form a bicontinuous structure. The spontaneous method is specially used for the thermolabile component. Alternatively, a temperature-dependent spontaneous twist of non-ionic surfactant is used for phase transition during the phase inversion method. The emulsion formed at phase inversion temperature will be reversed on cooling with continuous stirring. This process is also limited to incorporate the thermolabile component,



although limitation takes as approach decreased phase inversion temperature by suitable selecting surfactant (Lovelyn and Attama, 2011).

#### **High energy emulsification method:**

Apply high shear force energy to rupture the internal phase in the nanosized droplet by high-pressure homogenizers, ultrasonicator. In this method, required to input external energy to develop the formulation. Due to the presence of external energy formulation become unstable (Qian and McClements, 2011).

### **EVALUTION FOR MICROEMULGEL**

#### **Evaluation for Microemulsion**

##### **Droplet size microemulsion**

Globule size distribution of microemulsion is determined by using particle size analyzer (Ashara et al., 2016).

##### **Zeta potential measurement**

It's used to measure the charge on droplet. In conventional emulsion, charge on oil droplet is negative due to presence of fatty acid (Ashara et al., 2016).

##### **Viscosity**

Viscosity of prepare emulsion measure by Brookfield viscometer (Chincholkar et al., 2016).

##### **Centrifugation**

It is used to evaluate physical stability of microemulsion centrifuge at 5000 rpm for 10 min at ambient temperature and evaluate for creaming and phase separation visually (Chincholkar et al., 2016).

##### **Conductivity measurement**

Conductivity measurement gives idea about type of microemulsion if formed, weather it is oil in water or water in oil emulsion visually (Purohit et al., 2016).

#### **Evaluation for Microemulgel**

##### **Physical Examination**

Microemulgel were inspected for colour, homogeneity, consistency, texture and pH. pH of microemulgel measured by pH meter by making 1% of aqueous solution of formulated microemulgel (Sathe et al., 2015).

##### **Rheological Studies**

Mainly viscosity determine by cone and plate viscometer with spindle 52 at temperature  $25 \pm 1^\circ\text{C}$  using temperature (Sathe et al., 2015).

##### **Syneresis measurement test**

Upon standing sometimes gel system get shrinks a bit and little liquid is pressed out. This phenomenon

is known as Syneresis. In this test, microemulgel put in a cylindrical plastic tube with a perforated bottom which and covered with filter paper out after some time. In the cylindrical plastic tube liquid which separate from microemulgel will weigh. Percentage of Syneresis calculated as follow: % of Syneresis =  $\frac{\text{Weight of liquid separated from microemulgel}}{\text{Total Weight of microemulgel before centrifugation}} \times 100$

##### **Spreadability measurement**

Spreadability measures by slip and drag characteristic. It is determined by such apparatus, which consist of wooden block, pulley at one side end and two same dimensional glass slides. One slide attach to wooden called as ground slide. on ground slide place 1gm of emulgel and above place another glass slide, so emulgel become sandwich between these slide. 1kg wt place on these two slide for 5 minute to expel air out and provided uniform film between slide excess of emulgel scrapped off from edges. Then upper slide subjected to pull a definite weigh with the help of string attached to the hook. Measure time required by top slide to cover a distance of 7.5 cm shorter interval indicate better spreadability (Nandgude et al., 2008).

##### **Extrudability study**

Measure force required extruding the material from tube. It is determined by weight required to extrude 0.5 cm ribbon of emulgel in 10 sec from aluminum tube. If tube extruded more quantity it is better extrudability. Extrudability =  $\frac{\text{weight applied to extrude emulgel from tube (gm)}}{\text{Area (cm}^2\text{)}}$ .

##### **Drug content determination**

Drug content of gel will be measured by dissolving 1gm of gel in soluble solvent and Sonicate to mix well. Absorbance will be measured after dilution at  $\lambda$  max by using UV spectrometer. Standard plot of drug is prepared in same standard plot by putting the value of absorbance in standard plot equation. Drug content =  $(\text{concentration} \times \text{dilution factor} \times \text{volume taken}) \times \text{conversion factor}$  (Nandgude et al., 2008).

##### **In vitro diffusion study**

Franz diffusion cell (with effective diffusion area  $3.14\text{cm}^2$  and 15.5ml cell volume) used for drug release studies with 7.4 phosphate buffer solution. Withdraw specific quantity of sample at specific time interval (Nandgude et al., 2008).

##### **Stability studies**

Emulgel stability studies at  $5^\circ\text{C}$ ,  $25^\circ\text{C}$ , 60%, RH, and  $40^\circ\text{C}/76$  RH for a period of 3 month.

## CONCLUSIONS

To overcome the drawbacks and unwanted side effects of oral and/or parenteral routes, need to explore topical route. To overcome another issues like poor solubility of drug moieties/phytoconstituents in water as well as problem of penetration need of drug delivery systems like microemulgels. Components of microemulgels like oil, emulsifiers and co-emulsifiers are selected based on solubility of it in them, so the problem of solubility would be overcome and deposition of drug moieties at the site will be enhanced which Results in more therapeutic activity and Stability.

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## Conflict of Interest

The authors declare that they have no conflict of interest for this study.

## REFERENCES

- Akbari, J., Saeedi, M., Farzin, D., Morteza-Semnani, K., Esmaili, Z. 2015. Transdermal absorption enhancing effect of the essential oil of *Rosmarinus officinalis* on percutaneous absorption of Na diclofenac from topical gel. *Pharmaceutical Biology*, 53(10):1442-1447.
- Amin, S., Kohli, K., Khar, R. K., Mir, S. R., Pillai, K. K. 2008. Mechanism of In Vitro Percutaneous Absorption Enhancement of Carvedilol by Penetration Enhancers. *Pharmaceutical Development and Technology*, 13(6):533-539.
- Ashara, K. C., Paun, J. S., Soniwala, M. M., Chavda, J. R., Mendapara, V. P., Mori, N. M. 2016. Microemulgel: an overwhelming approach to improve therapeutic action of drug moiety. *Saudi Pharmaceutical Journal*, 24(4):452-457.
- Beitz, J. M. 2005. Heparin-induced thrombocytopenia syndrome bullous lesions treated with trypsin-balsam of peru-castor oil ointment: a case study. *Ostomy/wound management*, 51(6):52-54.
- Chincholkar, A. M., Nandgude, T. D., Poddar, S. S. 2016. Formulation of in-situ gelling ophthalmic

drops of moxifloxacin. *World Journal of Pharmaceutical Research*, 5(11):712-725.

- Fei, L. U., Ding, Y. C., Ye, X. Q., Ding, Y. T. 2011. Antibacterial effect of cinnamon oil combined with thyme or clove oil. *Agricultural Sciences in China*, 10(9):1482-1487.
- Jäger, S., Laszczyk, M., Scheffler, A. 2008. A Preliminary Pharmacokinetic Study of Betulin, the Main Pentacyclic Triterpene from Extract of Outer Bark of Birch (*Betulae alba cortex*). *Molecules*, 13(12):3224-3235.
- Jing, F., An, X., Shen, W. 2003. The characteristics of hydrolysis of triolein catalyzed by wheat germ lipase in water-in-oil microemulsions. *Journal of Molecular Catalysis B: Enzymatic*, 24-25:53-60.
- Karpanen, T. J., Conway, B. R., Worthington, T., Hilton, A. C., Elliott, T. S., Lambert, P. A. 2010. Enhanced chlorhexidine skin penetration with eucalyptus oil. *BMC Infectious Diseases*, 10(1).
- Lawrence, M. J., Rees, G. D. 2012. Microemulsion-based media as novel drug delivery systems. *Advanced Drug Delivery Reviews*, 64:175-193.
- Liu, W., Tian, R., Hu, W. 2012. Preparation and evaluation of self-microemulsifying drug delivery system of baicalein. *Elsevier*, 83:1532-1539.
- Lovelyn, C., Attama, A. A. 2011. Current State of Nanoemulsions in Drug Delivery. *Journal of Biomaterials and Nanobiotechnology*, 02(05):626-639.
- Malik, M. Z., Ahmad, M., Minhas, M. U., Munir, A. 2014. Solubility and Permeability Studies of Aceclofenac in Different Oils. *Tropical Journal of Pharmaceutical Research*, 13(3):327.
- McClements, D. J. 2012. Nanoemulsions versus microemulsions: terminology, differences, and similarities. *Soft Matter*, 8(6):1719-1729.
- More, S. B., Nandgude, T. D., Poddar, S. S. 2016. Vesicles as a tool for enhanced topical drug delivery. *Asian J Pharm*, 10:196-209.
- Nandgude, T., Thube, R., Jaiswal, N., Deshmukh, P., Chatap, V., Hire, N. 2008. Formulation and evaluation of pH induced in-situ nasal gel of salbutamol sulphate. *Int J Pharm Sci Nanotechnol*, 1:177-182.
- Phad, A. R., Nandgude, T. D., Ganapathy, S. 2018. Emulgel : A Comprehensive Review for Topical Delivery of Hydrophobic Drugs. *Asian J Pharm*, 2018(2):6-12.
- Priani, S. E., Humanisya, H., Darusman, F. 2012. Development of Sunscreen Emulgel Containing *Cinnamomum Burmannii* Stem Bark Extract. *International Journal of Science and Research (IJSR)*, 3(12):2338-2341.

- Purohit, D., Nandgude, T. D., Poddar, S. S. 2016. Nano-Lipid Carriers (NLC) For Topical Application: Current Scenario. *Asian Journal of Pharmaceutics*, 9(5):1-9.
- Qian, C., McClements, D. J. 2011. Formation of nanoemulsions stabilized by model food-grade emulsifiers using high-pressure homogenization: Factors affecting particle size. *Food Hydrocolloids*, 25(5):1000-1008.
- Sathe, S., Bagade, M., Nandgude, T., Kore, K., Shete, R. 2015. Formulation and evaluation of thermo reversible in-situ nasal gel of terbutaline sulphate. *Indo Am J Pharm Res*, 5:3680-3687.
- Shah, K. K., Shiradkar, M. R., Bindu, V. H. 2011. Transdermal delivery of aceclofenac: Effect of piperine and its mechanism of action. *Int. J. Pharma Bio Sci*, 2:10-18.
- Shahin, M., Hady, S. A., Hammad, M., Mortada, N. 2011. Novel Jojoba Oil-Based Emulsion Gel Formulations for Clotrimazole Delivery. *AAPS Pharm-SciTech*, 12(1):239-247.
- Silva, H., Cerqueira, M., Engineering, A.-J. O., Food 2015. Influence of surfactant and processing conditions in the stability of oil-in-water nanoemulsions. *Part B*, 167:89-98.
- Thakur, S., Thakur, N., Ghosh, N. 2016. Formulation and in-vitro evaluation of Polyherbal Microemulgel containing *Tinospora cordifolia* and Curcumin for treatment of Arthritis. *International Journal of Pharmaceutical Sciences and Drug Research*, 8(05):259-264.
- Yi, Q. F., Yan, J., Tang, S. Y., Huang, H., Kang, L. Y. 2016. Effect of borneol on the transdermal permeation of drugs with differing lipophilicity and molecular organization of stratum corneum lipids. *Drug Development and Industrial Pharmacy*, 42(7):1086-1093.