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# INNOVATIONS IN MICROEMULSION TECHNOLOGY: A STATE-OF-THE-ART APPROACH FOR TOPICAL DRUG DELIVERY

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## Abstract:

A topical drug delivery system usually denotes local dermatological activity as the effect of the pharmaceutical component on the skin to cure the disease. The microemulgel can be used to achieve a combined effect of microemulsion and gel. It shows the dual control release effect of drugs and increasing stability. It has the primary objective ability to incorporate hydrophobic drugs. Various market products containing foreign agent, for example gel, cream, ointment they have several drawbacks, including poor absorption, poor permeability, allergic reaction, irritation, less spreading stickiness, and stability problem. This evaluation provides a summary of the best properties, excipient, preparation, and evaluation related to microemulgel. A recent study of recent development and future directions for microemulgel-based systems was conducted. The emulgel provides various beneficial aspects of its cosmetic and dermatology activity, thixotropic, greaseless, emollient, easily distributed, readily removable, non-staining and water-soluble, with a long half-life, biocompatible, and transparent and pleasant appearing. Therefore, emulgel is a better semi-solid preparation neither conventional system nowadays. It is utilized to administer of anti-inflammatory, anti-fungal, anti-acne, analgesic, anti-psoriasis drugs. The formulated emulgel is characterized of various parameters such as pH, viscosity, spreadability, etc. its need and merit will advance in the upcoming years.

**Keywords:** Microemulgel, topical delivery, formulation, characterization, drug permeability, stability, applications.

## 1. Introduction

Skin applications are for the most part applied on human skin surfaces by different determinations like creams, moisturizers, gels, glues. They will use for both dermatological as well as cosmetics purposes. Other than the drug substance called non-medicated agents play an essential role in the pharmaceutical formulation by enhancing the solubility and stability of drug to be achieved pharmacological application. The number of doses can take through the skin

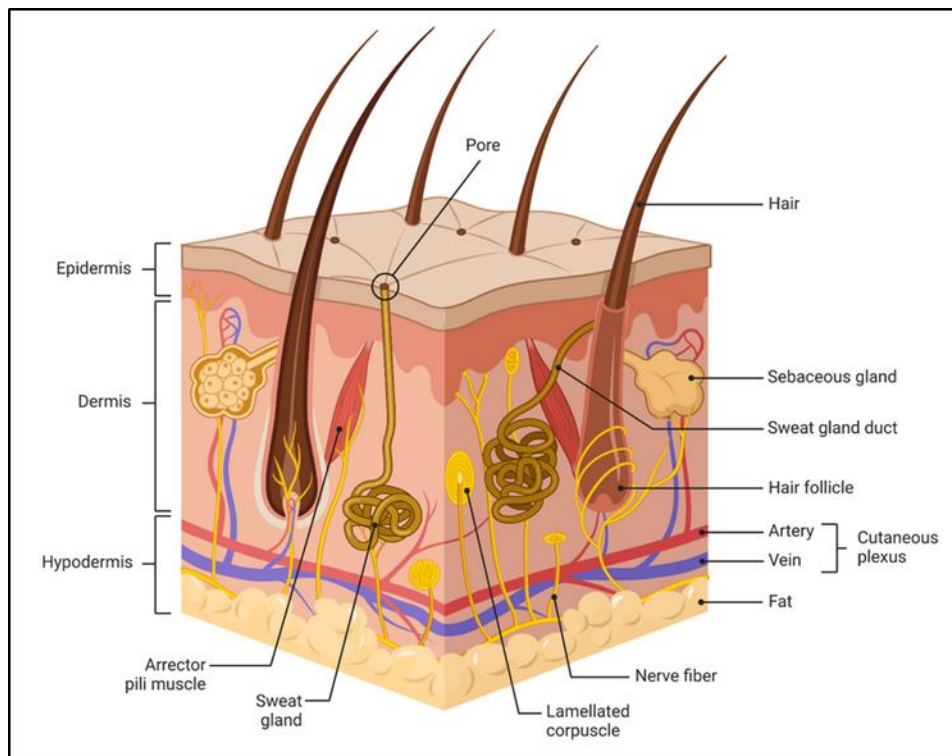


(topically), such as antifungals, antiseptics, skin emollients, and protectants. Nowadays, pharmaceutical research is primarily concerned with the patient's therapeutic needs (Calderon-jacinto *et al.*, 2022). However, because active pharmaceutical ingredients developed are hydrophobic, it is beneficial to form new hydrophobic drug delivery systems based on Microemulsions. The most commonly used drugs have side effects when administered orally, such as gastric irritation, nausea, gastrointestinal bleeding, etc (Tiwari *et al.*, 2022). To reduce systemic toxicity while simultaneously improving therapeutic outcomes, the skin is a promising route for administering a drug, Dermal drug delivery system is also known as a topical drug delivery system. Topically applied drug delivery systems are critical for achieving these advantages while controlling either maintaining effective moieties or enhancing customer acceptance. Topical applications of many moieties, which are widely used in the treatment of several diseases, are a substitute route for overcoming the disadvantages of the oral and rectal routes of administration. Hoar and Schulman pioneered the concept of micro-emulsions in the 1940s. It should be described as an optically isotropic and thermodynamically stable fluid miniature scattering network made out of water, oil, and an amphiphile. A micro-emulsion is a drug delivery vehicle that improves efficacy, bioavailability, and efficacy (Madawi *et al.*, 2023). Miniature emulsions are colloidal scatterings of oil and water that were thermodynamically constant, clear and circularly symmetric, have a low thickness, and are settled by an interfacial covering of emulsifiers. Micro-emulsions provide many benefits, including thermostability, the capacity to entrap both hydrophilic and hydrophobic medicinal substances, and soon (Agarwal *et al.*, 2021). In addition, they increase dermal mobility of chemical moieties due to lipophilicity and enhancing permeability due to surfactants. Formulation and development process, micro-emulsions require fewer unit operations, this is less expensive, requires less time, and is much more efficient. However, the thermodynamic activity of the drugs contained in the micro-emulsion has changed, modifying their partition co-efficient. As a result, its components, surfactants, and co-surfactants penetrate deeper into the stratum corneum, reduce the usable barrier of the stratum corneum. Microemulgel, a cross between a Microemulsion and a gel, gets all the benefits of both. Thixotropic, causeless, freely spreadable, freely washable, moist, non-staining, long life cycle, bio-friendly, clear, as well as appealing look like are a few of dermatological Emulgels' advantages. In addition, the drug's effective can be stopped at any time by removing formulation from the skin surface that cannot be performed by oral formulation (Gunarto *et al.*, 2022).

## 2. Physiology of skin

The vast majority of topical formulations have been applied to the skin. As a result, while formulating topical dose forms, elementary understanding the skin and its physiological behavior is essential. The tissue of a commonplace grown-up body has a surface place of around 2 m<sup>2</sup> and gets approximately 33% of the blood that circles all through the framework. Each square centimeter of human skin contains a normal of 40-70 hair follicles and 200-300 perspiration

channels. The pH of the skin goes from 4 to 5.6. The pH of the skin's surface is influenced by sweat and unsaturated fats delivered by sebum. The skin is made out of four diverse tissue layers (Crucianelli and Ehrsson 2023; Hirt *et al.*, 2019; Stamatias *et al.*, 2023).



**Figure 1:** Schematic representation for physiology of skin

**Non-viable epidermis:** The layer corneum is the skin outermost layer, and it fills in as an actual hindrance to most substances that come into contact with the skin. Over most of the body, the layer corneum is 10–20 cell layers thick. All cell is comprised of a level, plate-like design. 34–44  $\mu$ m long, 25–36  $\mu$ m in width, and 0.5–0.20  $\mu$ m in thickness with a surface space of 750–1200  $\mu$ m that are block-like stacked on top of one another. The top layer is generally comprised of lipids (5–15%), including phospholipids. Glycosphingolipids, cholesterol sulfate, an impartial lipid, and protein (75–85%), for the most part, keratin (Al-Amoudi *et al.*, 2005; Chacón *et al.*, 2023).

**Viable epidermis:** This skin layer, which lies between the stratum corneum and the corium, and its broadness of 60 to 99  $\mu$ m and contains the construction of the viable tissues. Tonofibrils connects cells. This area has a density similar to that of water. The content of moisture more than 90% (Knox *et al.*, 2022).



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**Dermis:** Just underneath the viable epidermis is the dermis. Only a few cells have structural fibrin, and only a few have identical features, it could be detected histologically in normal tissue. A matrix of loose connective tissue encoded by an amorphous group material with a thickness of 2000 to 3000 m makes up the dermis (Daly 1982; Mohamed and Hargest 2022).

**Subcutaneous connective tissue:** However, hypodermis, does not belong to the organized connective tissue, which is made up of white, fibrous connective tissue with a loose feel and contains blood and lymph vessels, sweat gland secretory stoma, and cutaneous nerves. Drugs that permeate the skin, according to most researchers, enter the circulatory system, fatty tissue may act as a drug depot before reaching the hypodermis (Zmener *et al.*, 2010).

**Role of Skin:** Human skin is the largest organ of the human body that can regulate body heat and water losses from skin's spores and prevent harmful chemicals and microorganisms enter into the body. It acts as a protective layer to the human body and covers up to 10% total body surface, approximately up to 1.7 m<sup>2</sup>. Because of extensive and accessible organ skin provides a larger surface area to the application of the drug to achieved both topical and systemic application (Firlej *et al.*, 2022).

**Table 1-** Investigating plant based ingredient for microemulgel formulation

S.no.	Name of the plant	Available compounds	Therapeutic constituents	Therapeutic effects	Plant part use	Formulation available	Reference
1	Antarctic plants	Flavonoids, flavones, and flavonols	—	UV absorber, sun protective activity, stimulate DNA-repair processes.	Aerial parts	—	(Pereira <i>c</i> 2009)
2	Buddleja cordata	Phenolic compounds	Verbascoside, linarin	Protect against UVB-induced skin damage, UV absorber, antioxidant	Leaves	—	(Avila Acevedo <i>et al.</i> , 2014)
3	Calendula officinalis	Polyphenol, flavonoid	Rutin, narcissin	Prevent UV irradiation-induced oxidative stress	Flower	Cream	(Fonseca <i>et al.</i> , 2010)
4	Calluna vulgaris	Flavonoids	—	Prevention/reduction of UV-induced skin damage and skin diseases, antiviral, antibacterial, antifungal, antioxidant activities, bioactive.	Entire plant	—	(Filip <i>et al.</i> , 2011)



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5	Camelia sinensis	Polyphenols	EC(-)-epicatechin, ECG(-)-picatechin-3-gallate, EGC(-)-epigallocatechin, EGCG(-)-epigallocatechin-3-gallate	Anticarcinogenic, anti-inflammatory, photostabilizing capacity	—	—	(Vayalil <i>et al.</i> , 2003)
6	Castanea sativa	—	—	Antioxidant	Leaf	Emulsion, semisolid,	(Almeida <i>et al.</i> , 2015)
7	Codium fragile	—	Clerosterol	Protection against UVB-induced pro-inflammatory and oxidative stress, antioxidant.	—	—	(Lee <i>et al.</i> , 2013)
8	Coffea genus	Lipid fraction	Linoleic acid, palmitic acid	UV absorber, emollient	Green dry coffee beans	—	(Wagemaker <i>et al.</i> , 2011)
9	Commiphora mukul	—	—	UV absorber	Resin	Tablet, gel, emulsion,	(S Kale <i>et al.</i> , 2013)
10	Crataegus pentagyna	Phenolic compounds, Flavonoids	—	UV absorber	Fruits	—	(S Kale <i>et al.</i> , 2013)



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11	Culcitium reflexum	Phenolic compounds, flavonols	Rutin, kaemp-ferol, quercetin and its glycosylated derivates, cinnamic acid derivates.	Antioxidant, reduces UVB-induced skin erythema, free radical scavenging effect.	Leaf	—	(Aquino <i>et al.</i> , 2002)
12	Cyclopia intermedia	Polyphenol	Hesperidin, mangiferin	Prevention/reduction of UV-induced skin damage and antioxidant, antimicrobial	—	—	(Petrova <i>et al.</i> , 2011)
13	Dracocephalum moldavica	Phenolic compounds flavonoids, flavon aglycone, tannins	Rosmarinic acid, caffeic acid, apigenin, luteolin	Sun protective activity, SFP N20, heart disease, atherosclerosis, migraine, neuralgia	—	Powder	(Khazaeli and Mehrabani 2008)
14	Eucheuma cottonii	K-carrageenan, flavonoids, phlorotannins	—	Antioxidant activity and protective effects against UV-induced ROS degeneration in keratinocytes	—	Cream,	(Lim <i>et al.</i> , 2015)
15	Fragaria x ananassa	Anthocyanins and hydrolyzable tannins	Pelargonidin	Antioxidant, reduces UVB-induced skin erythema, anti-inflammatory, diminishing DNA	Fruits	—	(Gasparrini <i>et al.</i> , 2015)



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				damage on UVA-induced skin damage			
16	Green Tea Extract				Green Tea Leaves	SLN, Thermosreversabe gel, tablet, cream, liquid, globule, kit, niosomal gel, capsule, chewing gum	(Y. Y. Lin <i>et al.</i> , 2021)
17	Glycine max	Polyphenolic compounds, polyisoprenylated benzophenone	Genistein	Antioxidant reduce skin photo damage and anticancer,	Seed	Tablet, gel, shampoo	(Figueiredo <i>et al.</i> , 2014)





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18	Ginger			anti-inflammatory, anti-oxidative, antithrombosis, and possible antiallergic effects	Root	Emulgel, nanoemulgel, capsule, powder, cream, gel, transdermal patch, nanoparticles, liposome, phytosomes	(Y. Y. Lin <i>et al.</i> , 2021)
19	Leontopodium alpinum	Lutein derivatives	Luteolin, glycosylated luteolin, hydroxyethylated luteolin, 3',4',5,7-tetralipoyloxyflavones, 5-hydroxy-3',4',7-trilipoyloxyflavones	UV absorber	—	Gel, cream	(Fischer <i>et al.</i> , 2011)
20	Moringa oleifera	Lipid fraction	—	UV absorber	Seeds	Gel, tablet, phytosomes, granules, cream	(Gaikwad and Kale 2011)



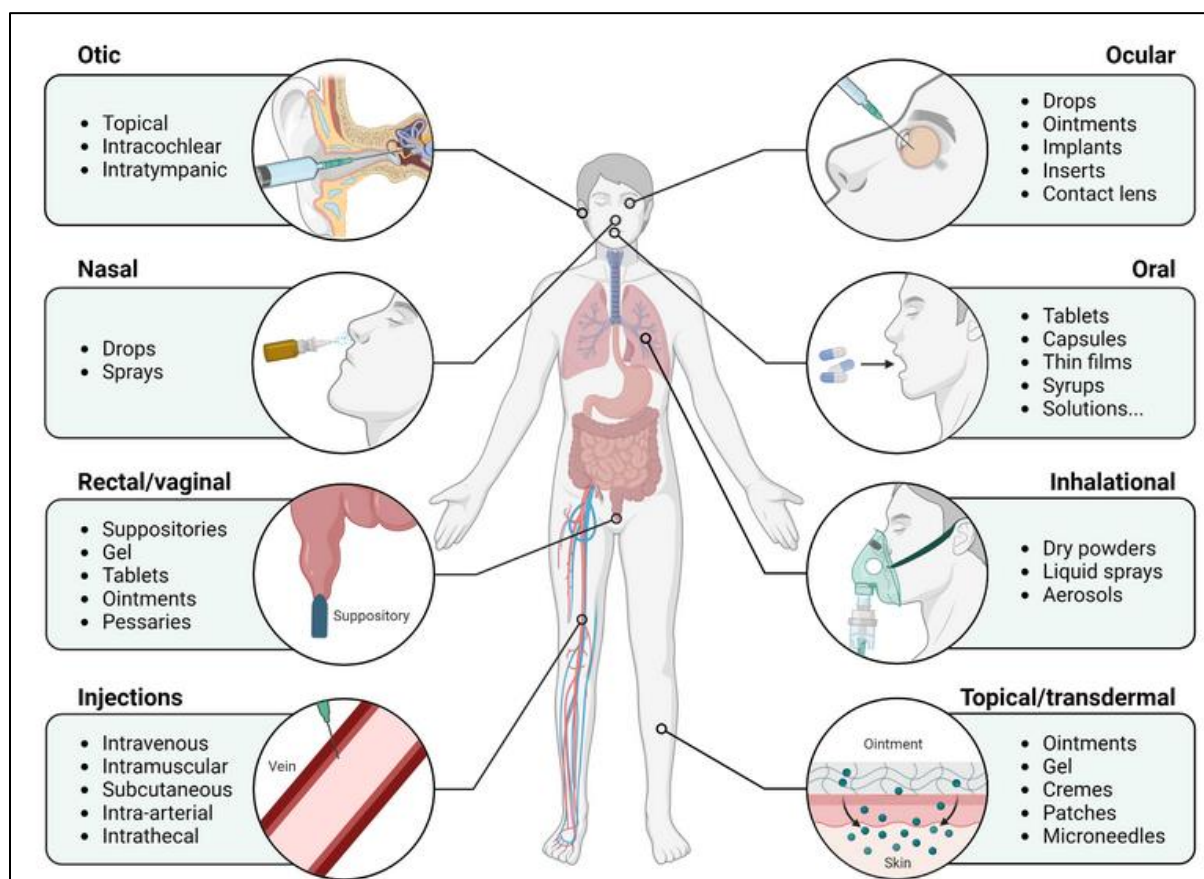
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21	Moringa concanensis, Nimmo	Lipid fraction	—	UV absorber, Sun protective activity	Seeds	—	(Shantanu Kale, Gajbhiye, <i>et al.</i> , 2010)
22	Neoglaziovia variegata	Flavonoids, phenolic compounds	Isoquercetin, kaempferol-3-O-rhamnoside, caffeic, protocatechuic, p-coumaric and vanillic acids	Photoprotective activity	Leaves and flowers	—	(Raimundo <i>et al.</i> , 2015)
23	Nigella sativa L	—	Linoleic acid, oleic acid, palmitic acid	Potential UV absorber	Seeds	—	(Cheikh-Rouhou <i>et al.</i> , 2007)
24	Ocimum basilicum	—	Linalool, methyl cinnamate, methyl linalool, methyl eugenol, citral, methyl chavicol, thymol, p-cymene, α-pinene	UV absorber	Leaf	—	(Shantanu Kale, Sonawane, <i>et al.</i> , 2010)

### 3. Topical drug delivery systems

Topical drug delivery systems are designed to deliver therapeutic agents directly to the site of action on the skin or mucous membranes. Conventional topical formulations include creams, ointments, gels, lotions, and transdermal patches. Each of these systems has its own advantages and limitations, influencing their selection based on the specific requirements of the drug, patient, and therapeutic goals (Bhowmik *et al.*, 2012; Kaur *et al.*, 2016).



**Figure 2: Schematic reorientation of Topical drug delivery systems**

**Creams:** Creams are semi-solid emulsions typically composed of water and oil phases stabilized by surfactants. They are easy to apply, spread evenly over the skin, and provide hydration. Creams are suitable for delivering both hydrophilic and lipophilic drugs. However, their efficacy may be compromised by the presence of preservatives and stabilizers, and they may be less occlusive compared to ointments (Konstantas *et al.*, 2019).



**Ointments:** Ointments are greasy, semi-solid formulations primarily composed of hydrocarbons or semisolid hydrocarbons. They provide an occlusive barrier that helps retain moisture and enhance drug penetration into the skin. Ointments are particularly beneficial for delivering lipophilic drugs and are ideal for conditions requiring long-term therapy. However, they may feel greasy and sticky, which can affect patient compliance (Wichaiyo *et al.*, 2023).

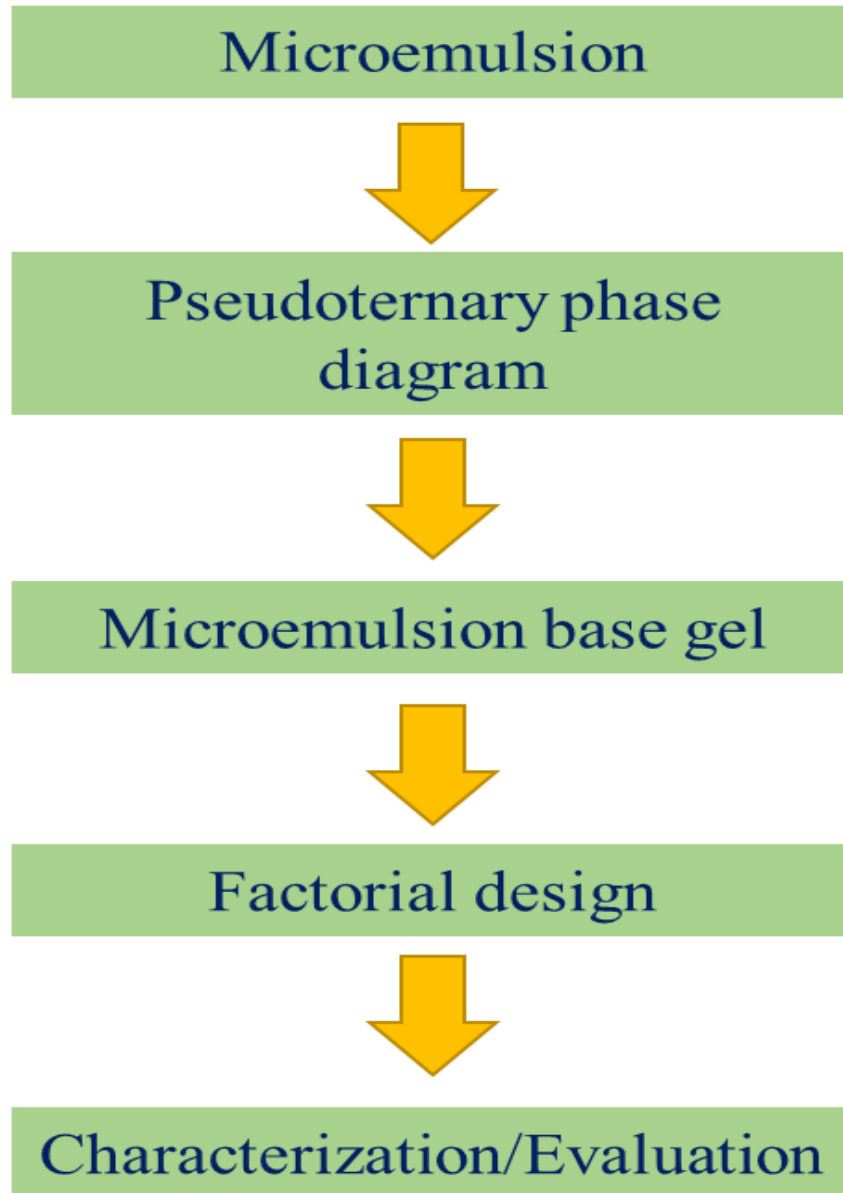
**Gels:** Gels are semi-solid systems composed of a three-dimensional network of polymers dispersed in a liquid phase. They exhibit properties intermediate between liquids and solids, offering advantages such as ease of application, non-greasy feel, and quick drying. Gels are suitable for delivering both hydrophilic and lipophilic drugs and are often preferred for localized drug delivery due to their ability to adhere to the skin and mucous membranes (PADMASRI *et al.*, 2020).

**Lotions:** Lotions are liquid formulations containing suspended or dissolved active ingredients. They are characterized by their low viscosity and high water content, making them suitable for covering large areas of the skin and providing cooling and soothing effects. Lotions are commonly used for moisturizing, cleansing, and delivering active ingredients such as anti-inflammatory agents and antipruritic (Kim *et al.*, 2021).

**Transdermal Patches:** Transdermal patches are adhesive patches containing drug reservoirs that deliver drugs through the skin for systemic absorption. They offer controlled release of drugs over an extended period, bypassing the first-pass metabolism and providing consistent plasma levels. Transdermal patches are convenient, non-invasive, and suitable for drugs with a narrow therapeutic index or requiring continuous delivery (Al Hanbali *et al.*, 2019).

#### 4. Microemulsions

Microemulsions are thermodynamically stable, isotropic liquid mixtures of oil, water, surfactant, and sometimes a co-surfactant. These systems form spontaneously and exhibit nanometer-scale droplets dispersed in a continuous phase. Microemulsions are characterized by their transparent or translucent appearance, low viscosity, and thermodynamic stability. Microemulsions typically consist of three main components: oil, water, and surfactant. In some cases, a co-surfactant is added to stabilize the system and decrease interfacial tension (Mariyate and Bera 2022). Microemulsions are formed through the spontaneous mixing of oil, water, and surfactant/co-surfactant at appropriate ratios. The surfactant molecules orient themselves at the oil-water interface, lowering interfacial tension and facilitating the formation of nanoscale droplets. Microemulsions exhibit several advantageous properties for drug delivery, including high solubilization capacity for both hydrophilic and lipophilic drugs, enhanced drug permeation through biological barriers, improved stability against coalescence and phase separation, and ease of formulation and scale-up (Souto *et al.*, 2022).



**Figure 3:** Basic component of microemulsion

**Table 2:** Different methods of microemulsion

S. No.	Method	Description	References
1	Phase Inversion	This method involves the spontaneous phase inversion of an oil-in-water (O/W) or water-in-oil (W/O) microemulsion system by changing the composition of the surfactant, co-surfactant, and water phase. It can be further classified as PIT (Phase Inversion Temperature) or PIS (Phase Inversion Composition) methods.	(Geleta <i>et al.</i> , 2023)
2	High-Energy	High-energy methods such as ultrasonication, high-pressure homogenization, and microfluidization are used to prepare microemulsions by applying mechanical energy to break down the components into smaller droplets and promote their dispersion.	(Yuan <i>et al.</i> , 2021)
3	Spontaneous	Spontaneous emulsification involves the formation of microemulsions without external energy input. This method relies on the self-assembly of surfactant molecules at the oil-water interface, driven by the interfacial tension reduction, leading to the formation of thermodynamically stable microemulsions.	(Zítek <i>et al.</i> , 2022)
4	Solvent Evaporation	This method involves dissolving the drug and components (surfactant, co-surfactant, oil, and water) in a volatile organic solvent, followed by its evaporation under reduced pressure or gentle heating to form a microemulsion. The resulting residue is reconstituted with an aqueous phase to obtain the final formulation.	(O'Donnell and McGinity 1997)

5	Phase Inversion Temperature (PIT)	The PIT method involves gradually heating or cooling the microemulsion components while monitoring the phase behavior until a phase inversion occurs. This method is particularly useful for systems exhibiting a phase inversion temperature, where the microemulsion type changes from O/W to W/O or vice versa.	(Jintapattanakit 2018)
6	Phase Inversion	This method involves the spontaneous phase inversion of an oil-in-water (O/W) or water-in-oil (W/O) microemulsion system by changing the composition of the surfactant, co-surfactant, and water phase. It can be further classified as PIT (Phase Inversion Temperature) or PIS (Phase Inversion Composition) methods.	(Perazzo <i>et al.</i> , 2015)

## 5. Gels

Gels are semi-solid systems composed of a three-dimensional network of polymers dispersed in a liquid phase. They exhibit properties intermediate between liquids and solids, offering advantages such as ease of application, non-greasy feel, and quick drying. Gels can be classified based on the nature of the polymer network into hydrogels (water-based gels) and organogels (oil-based gels). Gels consist of three main components: polymer network, solvent (aqueous or organic), and additives (such as gelling agents, stabilizers, and preservatives). The polymer network provides mechanical strength and controls the rheological properties of the gel (PADMASRI *et al.*, 2020). Gels are formed through the dispersion or dissolution of polymer molecules in the solvent, followed by the formation of a three-dimensional network through physical or chemical crosslinking. The gelation process can be triggered by factors such as temperature, pH, and concentration. Gels exhibit unique properties that make them suitable for a wide range of applications, including high water content, biocompatibility, transparency or opacity depending on formulation, ease of application and removal, and tunable rheological properties (e.g., viscosity, elasticity, and thixotropy) (Owens *et al.*, 2016).

## 6. Characterization Techniques

Physicochemical characterization plays a crucial role in understanding the properties of microemulgels, aiding in formulation optimization, stability assessment, and performance evaluation. Here are some key physicochemical characterization techniques commonly employed for microemulgels:

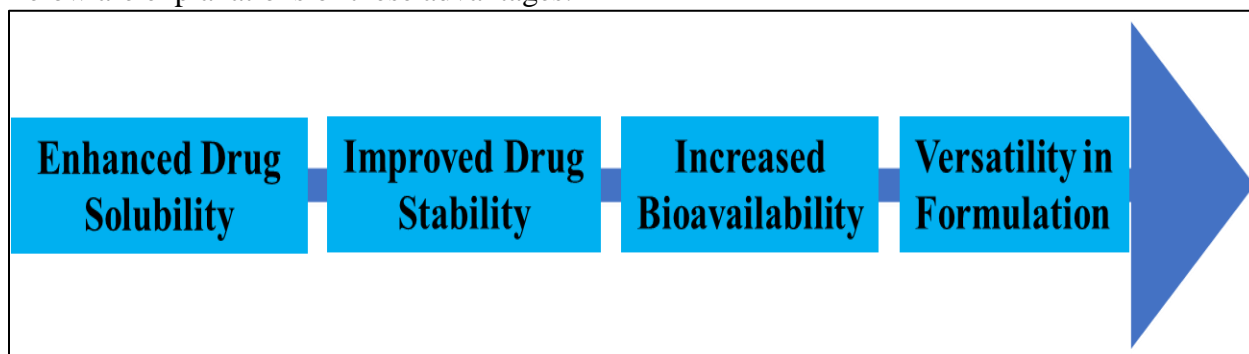


1. **Visual Appearance and Homogeneity:** Visual inspection involves assessing the appearance of microemulgels for characteristics such as color, transparency, and homogeneity. Any signs of phase separation, sedimentation, or visible particles should be noted (J. Li *et al.*, 2016).
2. **Droplet Size and Distribution:** Dynamic Light Scattering (DLS): DLS measures the size distribution of dispersed droplets in microemulsions within the nanometer range. It provides information on the mean droplet size, polydispersity index (PDI), and stability of the formulation (Chen and Ashgriz 2022).
3. **Microscopy Techniques:** Transmission Electron Microscopy (TEM) or Scanning Electron Microscopy (SEM) allows for direct visualization of droplet morphology, size, and distribution in microemulgels (Glatzel and Schimmel 2016).
4. **Rheological Properties:** Rheological characterization assesses the flow behavior and mechanical properties of microemulgels, which are essential for their application and stability. Rheological tests include viscosity measurements, shear rate profiles, and oscillatory tests (e.g., storage modulus, loss modulus, and complex viscosity), providing information on gel strength, thixotropic behavior, and structural stability (Bird *et al.*, 1982).
5. **Drug Content and Uniformity:** The drug content of microemulgels is determined using analytical techniques such as high-performance liquid chromatography (HPLC) or ultraviolet-visible (UV-Vis) spectroscopy. These tests ensure uniform distribution of the drug within the microemulgel formulation, assessing batch-to-batch consistency (Hamdan and Husian 2017).
6. **Physical Stability:**
  - a) **Centrifugation Test:** Microemulgels undergo centrifugation to evaluate their physical stability against phase separation, creaming, or sedimentation. Any changes in appearance or phase separation after centrifugation are observed (Shara *et al.*, 2018).
  - b) **Freeze-Thaw Cycling:** Microemulgels are subjected to multiple cycles of freezing and thawing to assess their stability under temperature variations (Ratnah *et al.*, 2023).
7. **In vitro Drug Release Studies:**
  - a) **Franz Diffusion Cell:** In vitro drug release studies are conducted using Franz diffusion cells with synthetic or biological membranes to simulate drug release and permeation through the skin (Sellami *et al.*, 2022).
  - b) **Dissolution Testing:** Dissolution tests evaluate the release profile of drugs from microemulgels using appropriate dissolution media and apparatus (Shtansky *et al.*, 2022).
8. **Physicochemical Properties:**
  - a) **pH Measurement:** The pH of microemulgels is measured to ensure compatibility with the skin and stability of active ingredients (Zhu *et al.*, 2008).
  - b) **Density and Refractive Index:** These properties provide information on the physical characteristics and composition of microemulgels (R. Dabhi *et al.*, 2011). Physicochemical characterization of microemulgels using these techniques enables comprehensive understanding of their formulation attributes, stability, drug release behavior, and performance as topical delivery systems (Liu *et al.*, 2015).



## 7. Advantages of Microemulgels

Enhanced drug solubility and stability are significant advantages offered by microemulsions, making them attractive for various pharmaceutical and cosmetic applications (G. *et al.*, 2021). Below are explanations of these advantages:



**Figure 4:** Advantages of Microemulgels

- a) **Enhanced Drug Solubility:** Microemulsions provide a unique environment where both hydrophilic and lipophilic drugs can be solubilized effectively. The presence of surfactants and co-surfactants in microemulsions reduces the interfacial tension between oil and water phases, leading to the formation of small droplets with large interfacial areas. This increased interfacial area enhances drug solubility by providing more contact between the drug molecules and the solvent. As a result, drugs that are poorly soluble or insoluble in either aqueous or lipid phases can be efficiently solubilized in microemulsions (Maggi *et al.*, 2023; Yousaf *et al.*, 2019).
- b) **Improved Drug Stability:** Microemulsions offer enhanced stability to encapsulated drugs due to their unique structure and composition. The presence of surfactants and co-surfactants in microemulsions helps to reduce interfacial tension and prevent phase separation. The small droplet size in microemulsions minimizes drug precipitation and aggregation, thereby enhancing drug stability. Additionally, the encapsulation of drugs within the oil or aqueous phase of microemulsions can protect them from degradation by environmental factors such as light, oxygen, and pH changes. Moreover, the thermodynamic stability of microemulsions ensures that the formulation remains homogeneous and stable over time, even under various storage conditions (Zheng *et al.*, 2020).
- c) **Increased Bioavailability:** The enhanced solubility and stability of drugs in microemulsions lead to improved bioavailability upon topical or oral administration. Solubilized drugs can more readily permeate biological barriers such as the skin or gastrointestinal tract, resulting in higher absorption and bioavailability. Microemulsions also facilitate rapid and uniform distribution of drugs within biological tissues, leading to more consistent and predictable pharmacokinetic profiles. This increased bioavailability allows for lower doses of drugs to achieve therapeutic

efficacy, reducing the risk of adverse effects and improving patient compliance (Ghosh *et al.*, 2021).

- d) Versatility in Formulation:** Microemulsions offer versatility in formulation design, allowing for the incorporation of a wide range of drugs with varying physicochemical properties. They can be tailored to meet specific therapeutic needs by adjusting the composition, droplet size, and rheological properties of the formulation. Additionally, microemulsions can accommodate various routes of administration, including topical, oral, ocular, and parenteral routes, making them suitable for diverse pharmaceutical and cosmetic applications (Dawoud *et al.*, 2023).

**Table 3: Advantages of Microemulgels**

S. No.	Advantage	Description	References
1.	Enhanced Drug Delivery	Microemulgels combine the advantages of both microemulsions and hydrogels, providing improved drug penetration through the skin barrier for enhanced therapeutic effects.	(Ke <i>et al.</i> , 2022)
2.	Dual Compatibility	The hybrid nature of microemulgels allows for the incorporation of both hydrophilic and hydrophobic drugs, expanding the range of therapeutic agents that can be delivered.	(Wu <i>et al.</i> , 2022)
3.	Prolonged Drug Release	Microemulgels offer controlled and sustained drug release kinetics, allowing for prolonged therapeutic action and reducing the frequency of application.	(Speer <i>et al.</i> , 2018)
4.	Improved Stability	The gel matrix of microemulgels enhances the stability of the formulation, preventing phase separation and degradation of active ingredients over time.	(Zhang <i>et al.</i> , 2022)
5.	Versatile Formulation	Microemulgels can be tailored to meet specific formulation requirements, allowing for customization of physicochemical properties such as viscosity and drug release profile.	(Schumacher <i>et al.</i> , 2021)
6.	Enhanced Patient Compliance	The ease of application and favorable sensory attributes (e.g., smooth texture, non-greasy feel) of microemulgels improve patient acceptance and compliance with therapy.	(Mohammed <i>et al.</i> , 2016)

## 8. Applications of Microemulgels

Microemulgels, combining the benefits of microemulsions and gels, have found diverse applications in pharmaceutical, cosmetic, and personal care industries (Salabat and Parsi 2021). Here are some key applications:

- a) **Topical Drug Delivery:** Microemulgels are extensively used as carriers for topical drug delivery due to their enhanced solubility, stability, and permeability. They can deliver a wide range of drugs including anti-inflammatory agents, analgesics, antibiotics, antifungals, and antioxidants for the treatment of various skin conditions such as eczema, psoriasis, acne, and fungal infections. The controlled release properties of microemulgels can provide sustained drug delivery, minimizing the frequency of application and improving patient compliance (Beheshti-Mall *et al.*, 2018).
- b) **Transdermal Drug Delivery:** Microemulgels are employed for transdermal drug delivery to achieve systemic absorption of drugs while bypassing the first-pass metabolism. They enable the permeation of drugs through the skin barrier, allowing for the delivery of both hydrophilic and lipophilic drugs with improved bioavailability. Transdermal microemulgel formulations can be used for the delivery of hormones, analgesics, cardiovascular drugs, and other therapeutic agents (G. *et al.*, 2021).
- c) **Cosmeceutical Formulations:** Microemulgels are utilized in cosmetic formulations for skincare and dermatological applications. They can deliver active ingredients such as vitamins, antioxidants, moisturizers, and anti-aging agents to improve skin health, hydration, and appearance. Microemulgels are incorporated into creams, lotions, serums, and masks for their light texture, non-greasy feel, and ability to enhance skin permeation of active ingredients (Tessema *et al.*, 2021).
- d) **Sunscreen Formulations:** Microemulgels serve as effective vehicles for sunscreen formulations due to their ability to solubilize both hydrophobic and hydrophilic UV filters. They provide uniform distribution of UV filters on the skin, ensuring adequate protection against harmful UV radiation. Microemulgel-based sunscreens offer enhanced stability, water resistance, and skin compatibility compared to conventional sunscreen formulations (Sari *et al.*, 2023).
- e) **Wound Healing and Scar Management:** Microemulgels containing growth factors, peptides, and anti-inflammatory agents are used for wound healing and scar management. They promote tissue repair, reduce inflammation, and minimize scar formation by delivering therapeutic agents directly to the wound site. Microemulgels offer advantages such as ease of application, non-staining properties, and improved patient comfort during wound care (Okur *et al.*, 2020).
- f) **Personal Care Products:** Microemulgels are incorporated into personal care products such as hand sanitizers, moisturizing creams, and shaving gels. They provide desirable sensory attributes, including smooth texture, quick absorption, and non-sticky feel, enhancing user experience and product acceptance. Microemulgel-based personal care products offer improved stability, aesthetics, and efficacy compared to conventional formulations (Azeem *et al.*, 2008).

- g) Skincare Formulations:** Microemulgels have gained significant attention in the cosmetic industry for their versatile applications in skincare and sunscreen formulations (Alesandra Stinghen Garcia Lonni *et al.*, 2022). Here's how microemulgels are utilized in these cosmetic application:
- I. **Moisturizers:** Microemulgels are commonly used as moisturizers due to their ability to deliver hydration and active ingredients to the skin effectively. They provide a lightweight and non-greasy texture, making them suitable for daily use (Chaiyana *et al.*, 2016).
  - II. **Serums and Essences:** Microemulgels are incorporated into serums and essences to deliver concentrated doses of active ingredients such as vitamins, antioxidants, and peptides. They enhance the penetration of these ingredients into the skin, promoting skin health and rejuvenation (Anonymous. 2015).
  - III. **Anti-aging Products:** Microemulgels containing anti-aging agents such as retinoids, hyaluronic acid, and collagen peptides are used to reduce wrinkles, fine lines, and other signs of aging. They provide targeted delivery of active ingredients to the deeper layers of the skin, enhancing their efficacy (Rattanachitthawat *et al.*, 2022).
  - IV. **Acne Treatments:** Microemulgels can deliver acne-fighting ingredients such as salicylic acid, benzoyl peroxide, and niacinamide to treat acne and prevent breakouts. They offer controlled release of these ingredients, minimizing irritation and dryness commonly associated with acne treatments (Wani *et al.*, 2018).
- h) Sunscreen Formulations:** Microemulgels are widely used as vehicles for sunscreen formulations due to their ability to solubilize both hydrophobic and hydrophilic UV filters. They provide uniform distribution of UV filters on the skin, ensuring broad-spectrum protection against UVA and UVB radiation. Microemulgel-based sunscreens offer enhanced stability, water resistance, and skin compatibility compared to conventional sunscreen formulations. These formulations are available in various formats such as lotions, creams, sprays, and sticks, catering to different preferences and skin types (Yang *et al.*, 2017).
- i) Skin Whitening Products:** Microemulgels are employed in skin whitening products to deliver active ingredients such as hydroquinone, kojic acid, and arbutin. They facilitate the penetration of these ingredients into the skin, inhibiting melanin production and reducing hyperpigmentation. Microemulgels offer targeted delivery of skin-lightening agents to specific areas of concern, such as dark spots and uneven skin tone, resulting in brighter and more even complexion (C.-C. Lin *et al.*, 2016).
- j) Anti-inflammatory and Soothing Formulations:** Microemulgels containing anti-inflammatory and soothing ingredients such as aloe vera, chamomile extract, and panthenol are used to calm and soothe irritated or sensitive skin. They provide a gentle and hydrating formulation that helps alleviate redness, itching, and discomfort associated with various skin conditions such as eczema, dermatitis, and sunburn (Reis *et al.*, 2017).



## 9. Challenges and Future Perspectives

Challenges and future perspectives for microemulsions are intertwined with the complexities of achieving stability, scalability, and regulatory compliance while unlocking their full potential across diverse applications. Long-term stability remains a significant challenge, requiring innovative approaches to mitigate issues such as phase separation and Ostwald ripening. Scale-up from lab to industrial production poses hurdles in maintaining quality and cost-effectiveness (K. Li *et al.*, 2021). Regulatory considerations demand rigorous safety assessments and adherence to standards for approval and commercialization. Moreover, addressing formulation complexity and biocompatibility concerns while minimizing environmental impact is paramount. Future perspectives lie in advancing manufacturing processes, understanding interfacial dynamics, and exploring multifunctional excipients to tailor rheological properties (Pal *et al.*, 2018). Novel applications beyond drug delivery and cosmetics beckon, calling for collaboration and knowledge exchange to propel microemulsion technology into new frontiers (Xu *et al.*, 2020).

## 10. Conclusion

In conclusion, the emergence of microemulgels represents a significant advancement in the field of topical drug delivery. This novel hybrid system combines the advantages of both microemulsions and hydrogels, offering enhanced stability, improved skin permeation, and prolonged drug release. The synergy between the microemulsion and hydrogel components allows for the efficient incorporation of both hydrophilic and hydrophobic drugs, expanding the range of therapeutic agents that can be delivered via this platform. The application of microemulgels holds great promise across various fields including dermatology, cosmeceuticals, and pharmaceuticals. Their ability to penetrate the skin barrier and deliver drugs directly to the target site makes them particularly valuable for treating dermatological conditions such as acne, eczema, and psoriasis. Additionally, microemulgels can be tailored to control the release kinetics of active ingredients, providing sustained and localized therapy while minimizing systemic side effects. Furthermore, the versatility of microemulgels allows for customization of their physicochemical properties to meet specific formulation requirements. Various techniques such as particle size manipulation, selection of surfactants and co-surfactants, and optimization of the gel matrix composition can be employed to fine-tune the characteristics of microemulgels for optimal performance. Despite these advancements, several challenges remain to be addressed in the development and commercialization of microemulgels. These include optimizing formulation parameters to ensure reproducibility and scalability, as well as conducting comprehensive

stability and safety assessments to meet regulatory requirements. In conclusion, microemulgels represent a promising platform for topical drug delivery, offering numerous advantages over traditional dosage forms. Continued research and development in this area are warranted to fully realize the potential of microemulgels in improving therapeutic outcomes and patient care.

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