A Review On: Microemulgel as a Topical Drug Delivery System

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Abstract

Microemulgels have appeared as a hopeful topical drug delivery system, combining the advantages of microemulsions and hydrogels. This review aims to provide an overview of microemulgels as an efficient and versatile platform for delivering drugs through the skin. Microemulgels are thermodynamically stable, transparent, as well as isotropic systems composed of oil, water, surfactant, and co-surfactant, with the addition of a gelling agent. They exhibit unique properties such as improved drug solubility, enhanced permeation, controlled release, and increased stability. These characteristics make microemulgels proper for delivering a extensive assortment of therapeutic agents, together with hydrophobic as well as hydrophilic drugs, proteins, and peptides. The combination of microemulsions and hydrogels in microemulgels offers several advantages. Microemulsions provide high drug-loading capacity, rapid drug release, and improved skin penetration, while hydrogels offer viscosity, ease of application, and prolonged drug release. The integration of these two systems in a microemulgel provides a synergistic effect, resulting in enhanced drug delivery efficiency and therapeutic outcomes. Various techniques, including phase inversion temperature, spontaneous emulsification, and self-emulsification, have been employed for microemulgel formulation. Factors influencing their stability and performance, such as surfactant/co-surfactant selection, oil-to-water ratio, and gelling agent concentration, have been extensively investigated. Moreover, microemulgels offer flexibility in terms of administration routes, including topical, transdermal, and ocular applications. They can be tailored to achieve desired rheological properties, ensuring ease of application and patient compliance. In conclusion, microemulgels represent a promising approach for effective drug delivery through the skin. Their unique properties, versatility, and ability to encapsulate diverse therapeutic agents make them a valuable tool in pharmaceutical and cosmetic industries. Further research is needed to explore their full potential, optimize formulations, and evaluate their efficacy and safety in clinical settings.

Keywords: Micro-emulgel, Micro-emulsion, Topical drug delivery, Skin, Gel, Application.

Introduction

In recent decades, various methods have been utilized to treat disorders by administering medications through different routes such as oral, sublingual, rectal, and parenteral routes[1]. However, when it comes to localized skin infections like psoriasis, acne, and fungal infections, the topical drug delivery technique is often employed. This method involves applying a medication-containing formulation directly to the skin to treat cutaneous conditions. Researchers in the field of pharmaceuticals are currently focused on meeting the therapeutic needs of patients, particularly regarding hydrophobic drugs, as a majority of the active pharmaceutical components under investigation exhibit hydrophobic properties[2].

A unique organ that is essential to preserving life on Earth is the skin of a person. It controls heat and water loss from the body while acting as a barrier against harmful substances and pathogens. Ointments, creams, and lotions are commonly used topical agents, but they have certain drawbacks[3]. They can cause discomfort for patients due to their stickiness and often require rubbing during application due to their low spreading coefficient. Additionally, these preparations face stability issues as semisolid formulations. As a result, the usage of translucent gels has gained popularity in together pharmaceutical in addition to cosmetic preparations[3].

Topical gels have a high solvent with gelling component proportion and are semisolid formulations. Despite interconnecting three-dimensional chains of particulates or solvated macromolecules in the dispersed stage, they develop a semi-rigid structure known as a gel, which restricts the mobility of the dispersing medium. These gels offer several advantages, including non-invasiveness, high patient compliance, reduced greasiness, easy removal from the skin, cost-effectiveness, localized effects with minimal side effects, enhanced bioavailability, fewer required doses, and stable drug delivery patterns[4].

However, one significant limitation of gels is their effectiveness in delivering hydrophobic medications. To overcome this challenge, a microemulsion-based technique is being employed, allowing hydrophobic drug moieties to benefit from the special qualities of gels. This technique involves creating an oil-in-water microemulsion first, which is then mixed with a gelling agent to form a gel[5]. The resulting emulsified gel serves as a stable and efficient drug delivery system for water-insoluble or hydrophobic medications. In essence, microemulsion-based gels represent a hybrid approach that combines the advantages of both systems.

The use of topical treatments for fungal infections dates back many centuries. A wide range of medications and agents, including anesthetics, anti-inflammatory drugs, antiseptics, anti-

bacterial, antifungals, antivirals, anti-acne treatments, and skin emollients and protectants, are applied directly to the skin[5]. The primary advantage of the topical route is its ability to bypass the first-pass effect and deliver the medication directly towards the targeting tissue, such as the skin as well as mucous membranes, without undergoing significant metabolism in the first-pass organs. However, before a drug moiety from a topical formulation can penetrate the skin, it must go through several stages[6].

Topical drug delivery systems can be separated into two main subcategories: external topical and internal topical. Internal topical are administered orally, vaginally, otherwise applied to the rectal tissues in lieu of local action. On the other hand, external topical are spread, sprayed, before then applied to the affected area. Topical drug delivery systems offer several advantages, including evading first-pass metabolism, bypassing gastrointestinal illogicalities, targeted site-specific action, improved patient compliance, ease of self-medication, and the ability to quickly discontinue medication when necessary.

In summary, topical drug delivery techniques have been developed to effectively treat localized skin infections. Gels, especially those based on microemulsions, offer significant advantages as a drug delivery system, overcoming the limitations of traditional formulations.

Topical Drug Delivery System Classification[7, 8]

1. **Solid:** Powders
2. **semi-solid substances:** , ointments, and plasters Pastes, gels, creams, and other
3. **Liquid:** Paints, lotions, tinctures, solutions, emulsions, and suspensions.
4. **Miscellaneous:** Topical aerosol, tapes and gauze, rubbing alcohol, liquid cleanser, and transdermal medication delivery systems

The Advantages of Topical Drug delivery System[9, 10]

- Avoid the initial breakdown of drugs in the body's metabolism.
- User-friendly and straightforward to use.
- Eliminate the risks and drawbacks associated with intravenous therapy, as well as challenges related to absorption such as pH changes, enzyme presence, and stomach emptying time.
- Easily discontinue medication when needed.
- Deliver drugs with greater precision to specific target areas.
- Minimize gastrointestinal toxicity.
- Permit the administration of drugs with a constrained pharmacological range and brief biological half-life.
- Improve patient adherence to medication.

- Allow in lieu of self-medication capabilities.
- Achieve efficiency with a subordinate everyday dose of medication through incessant administration.
- Prevent fluctuations in drug levels among patients.
- Offer a broader range of application compared to the nasal or buccal cavities.
- Enable precise administration of medications to specific locations.

Disadvantages of Topical Drug Delivery System[11]

- The medication and accompanying ingredients can result in skin irritation or contact dermatitis.
- There is a possibility of allergic reactions.
- Enzymes present in the skin can cause the breakdown or inactivation of the medication.

Considerations impacting the drug's topical absorption biological aspects [12, 13]

- Thickness of the skin
- Skin's pH level
- Amount of lipids in the skin
- Blood circulation in the skin
- Moisture content of the skin
- Density of hair follicles
- Inflammatory state of the skin
- Presence of any skin diseases or conditions
- Density of sweat glands

Physiochemical factors[14]

- Impact of carrier substances
- Partition coefficient
- Size of molecules
- Degree of ionization (Only non-ionized drugs are well-absorbed).

Anatomy and Physiology of the Skin

The skin, which is readily accessible on the body's surface, plays a crucial role in delivering topical medications. It covers an approximate area of 20 square feet and serves to safeguard us against microbes, control body fever, and provide senses like touch, heat, and cold. The pH of the skin ranges since 4 to 5.6 and can be influenced by sweat and fatty acids produced by sebum[15,16]. The skin is composed of three layers, as depicted in Figure 1.The Epidermis

1. The Dermis
2. The Subcutaneous fat tissue

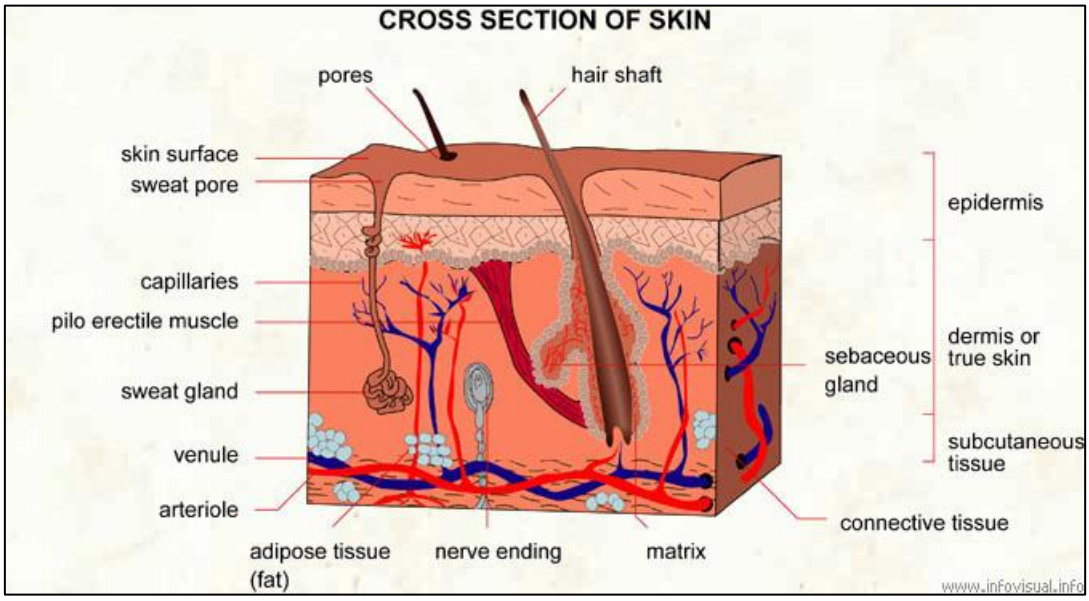

Figure 1: Structure and layer of human skin

1. **The epidermis:** The skin's outermost layer is made up of stratified squamous epithelial cells and is composed of 90% water. It is neither a capillary nor a blood vessel[17].

   Layers of epidermis[18]

   a. Stratum corneum (horny layer)
   b. Stratum germinativum (growing layer)
   c. Malpighi on layer (pigment layer)
   d. Stratum spinosum (prickly cell layer)
   e. Stratum lucidum
   f. Stratum granulosum (granular layer)

2. **The dermis:** The dermis, situated underneath the epidermis, consists of a linkage of elastic and collagen fibres embedded in a mucopolysaccharide matrix. It provides structural support and has a thickness ranging from 2000 to 3000 micrometers[19].
3. **The subcutaneous fat tissues:** The subcutaneous fat tissues, also identified as superficial fascia, connect the dermis towards the underlying structures. This layer is composed of

loose-textured, white, fibrous connective tissue containing adipose (fat) cells, along with cutaneous nerves, blood and lymphatic vessels, and sweat gland secretory pores[20].

4. Mechanism of Drug Absorption[21]

The following procedures are involved in drug permeation as shown in Figure 2:

1. Sorption of a penetrating molecule onto the stratum corneum's top layer.
2. Diffusion via it, reach the dermis, and viable epidermis.
3. The chemical enters the microcirculation and is distributed throughout the body.

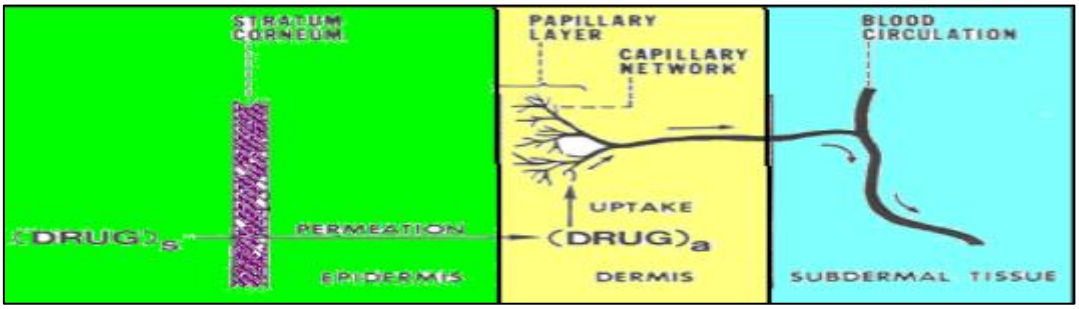

Figure 2: Multilayered skin illustration illustrating the order in which the drug permeates the skin

Routes for permeation

Two diffusional pathways are possible for a chemical to enter normally undamaged skin as shown in Figure 3[22].

1. **Appendageal pathway:** Conveyance through sweat glands and hair follicles through related sebaceous glands makes up the appendageal route[23].
2. **Epidermal route:** The transcellular and intercellular pathways are two possible micro routes of entry for medications that mostly traverse the horney layer.
    - Drugs that are trans-cellular can go across epithelial cells.
    - Intercellular: Drug delivery via the junction of epithelial cells[24].

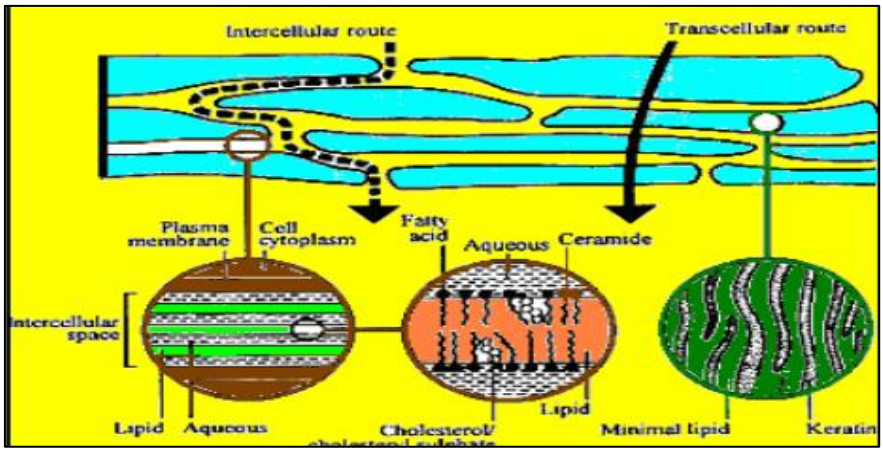

Figure 2: Epidermal routes for drug permeation

Introduction of Microemulsion Based Gel

Hoar and Schulman were the pioneers who initially proposed the concept of a microemulsion in the 1940s[25]. Meanwhile, the combination of gel and microemulsion led to the development of microemulgel. In recent years, there has been a significant focus on advancing drug delivery methods to address the limitations of traditional administration routes such as oral, sublingual, and rectal. Topical drug delivery systems are employed when these conventional methods fall short. These systems involve applying a drug-containing formulation directly towards the skin, aiming towards confining the medication's effects to the skin's surface. The current focus of pharmaceutical research is centered on meeting patient therapeutic needs, as many commonly used medications exhibit negative effects when taken orally, such as nausea, gastrointestinal bleeding, and stomach discomfort. Topical administration through the skin offers a potential solution to reduce systemic toxicities, minimize side effects, and achieve improved therapeutic outcomes[26].

Gels have been widely used as a delivery mechanism for topical medications due to their ease of administration and removal. However, gels have limitations in delivering hydrophobic drugs. To overcome this drawback, microemulgels have been developed, combining the unique properties of gels with the ability to effectively deliver hydrophobic drugs. Innovative polymers through complex purposes have garnered interest as emulsifiers and thickeners, enabling the formulation of stable emulsions and creams. The existence of a gelling agent in the aqueous phase transforms a conventional microemulsion into a microemulgel. Together water-in-oil and oil-in-water emulsions are utilized to create microemulgels for delivering hydrophilic and hydrophobic drugs to the skin. Microemulgels offer advantages such as enhanced drug solubility, easier drug migration, faster drug release, thixotropic properties, greaselessness, and ease of spreading and removal, emollience, non-staining, water solubility, extended shelf life, bio-friendliness, transparency, and an aesthetically pleasing appearance[27]. Microemulsions, composed of water, oil, surfactant, and/or co-surfactant, have shown promise in solubilizing poorly water-soluble drugs and improving their topical and systemic availability. These optically isotropic and thermodynamically stable systems facilitate the absorption of lipophilic drugs, making them beneficial for topical drug delivery. Carbopol 934 gel basis is often combined with microemulsion for prolonged skin contact. Topical and dermatological products play a crucial role in improving or restoring basic skin functions or pharmacologically modifying tissue activities. Ointments, creams, and lotions, commonly used as topical agents, have drawbacks such as stickiness, low spreading coefficient requiring rubbing, and stability issues. Transparent gels have gained popularity in pharmaceutical and

cosmetic preparations due to their advantages. However, hydrophobic drugs cannot be effectively delivered using gels alone. To navigate around the constraints, an emulsion-based methodology has been developed, allowing the incorporation and delivery of hydrophobic drugs within gels. Emulgel incorporates drug/oil/water emulsions into a gel base, providing enhanced drug stability and release[28].

Advantages of micro-emulsion-based gel[29]

Emulgels offer several advantages over other transdermal formulations:

Improved stability: Emulgels exhibit better stability compared to creams, ointments, and regular emulsions. They do not undergo phase inversion, breaking, or rancidity, providing enhanced stability.

Higher loading capacity: Emulgels have a superior drug loading capacity because of their extensive network, unlike nanosized formulations like noisomes and liposomes that may leak and have less effective trapping.

Cost-effective and feasible production: Emulgels can be manufactured using shorter and simpler procedures, without requiring specialized equipment. The materials used are inexpensive and readily available, resulting in lower production costs.

Incorporation of hydrophobic drugs: Hydrophobic drugs, especially class IV pharmaceuticals, face solubility barriers that hinder their direct incorporation into gel bases. Emulgel facilitates the incorporation of hydrophobic drugs by creating an oil-water emulsion, which can then be incorporated into a gel base, enhancing drug stability and release.

No intensive sonication: Unlike vesicular formulations, emulgels do not require vigorous sonication, which can cause medication leakage and degradation.

Controlled release: Emulgels enable controlled release, allowing for prolonged drug effects, particularly for drugs with shorter half-lives.

Enhanced drug effectiveness: Microemulsion delivery systems can increase a drug's effectiveness by minimizing problems associated with gastrointestinal absorption, such as pH variations, enzymatic activity, and interactions with food and beverages.

Improved absorption and bioavailability: Microemulsions penetrate the epidermal barrier at an enhanced rate, leading to improved drug absorption and bioavailability.

Defense against hydrolysis and oxidation: Drugs in the oil phase of oil-in-water microemulsions are shielded from water and oxygen, providing protection against hydrolysis and oxidation.

Non-greasy and easy to wash off: Emulgels have a less oily texture and can be easily washed off the skin.

Enhanced patient compliance: The non-invasive nature of microemulsion gels improves patient compliance.

Equivalent dose reduction compared to oral administration: Microemulsion gels allow for dose reduction while maintaining therapeutic effectiveness equivalent to oral administration.

Drawbacks of micro-emulsion based gel[30]

- Larger particle sizes of drugs pose challenges for their absorption through the skin.
- Some medications exhibit poor transdermal permeability.
- Transdermal delivery is suitable for drugs that exert their effects at very low concentrations in the bloodstream.
- There is a risk of potential allergic reactions. Enzymes present in the epidermis can potentially degrade the medications.

Component of microemulsion based gel[31]

Oil phase: The kind of oil selected depends on the drug along with the mode of administration. The screening oil must be able to saturate the drug in it. The oil has the ability to expand its surfactant tail group and influence curvature. Saturated and unsaturated fatty acids each have particular qualities that help with penetration. Another of the unsaturated fatty acids that significantly improves skin penetration is oleic acid. Recently, it has become more common to use semi-synthetic oils, because are more stable than their natural counterparts. To make an efficient o/w microemulsion system, drugs that are weakly soluble in water must be soluble in the dispersed oil phase. Even when oil concentration rises, the o/w microemulsion enlarges droplet size[32].

Aqueous phase: Preservatives and active substances that are hydrophilic may be present in the aqueous phase. Aqueous phases are most frequently made of water[33].

Surfactants: Surfactants' main function is to reduce interfacial tension to a very low level. This will help the microemulsion disperse and create a flexible film that can effortlessly deviate from surrounding droplets and have the right lipophilic characteristics in order to generate the right curvature at the interfacial region. Surfactants include the following for stabilizing microemulsion systems are:

- Non-ionic,
- Zwitterionic,
- Cationic, or
- Anionic

- The stability of a microemulsion is influenced by the interactions between the hydrophilic finish of the surfactant and the aqueous phase. These interactions differ depending on whether the surfactant is ionic or non-ionic. Ionic surfactants are furthermore become stable through the electrical double layer, while non-ionic surfactants rely on dipole and hydrogen bond interactions with the water's hydration layer on their hydrophilic surface. Consequently, the stability of an emulsion or microemulsion is more significantly influenced by ionic surfactants compared to non-ionic surfactants. However, due to concerns about toxicity, ionic surfactants are generally not recommended for pharmaceutical applications. Pharmaceutical formulations are frequently thought to be suited for non-ionic surfactants. According to common wisdom, low HLB (3-6) and high HLB (8-18) surfactants should be used for generating water-in-oil (w/o) and oil-in-water (o/w) microemulsions, respectively. To obtain the optimum range for microemulsion production, co-surfactants are occasionally needed to reduce the beneficial HLB of surfactants with a value above 20[34].

Co-surfactants: The effectiveness of single-chain surfactants in reducing the interfacial tension between oil and water is insufficient to create microemulsions independently. Co-surfactants are used to increase the interfacial film's flexibility and overcome this limitation, allowing the generation of microemulsions in a variety of compositions. The lipophilic chains of the surfactant must be sufficiently short or contain fluidizing groups, like unsaturated bonds when using a single surfactant film. Co-surfactants are frequently used to increase the fluidity of the interface and further lower the interfacial tension, including alcohols with short to medium chain lengths (C3-C8). As seen in the given Figure 4, common co-surfactants include short-chain alcohols (such as ethanol to butanol), glycols like propylene glycol, medium-chain alcohols, amines, and acids[35].

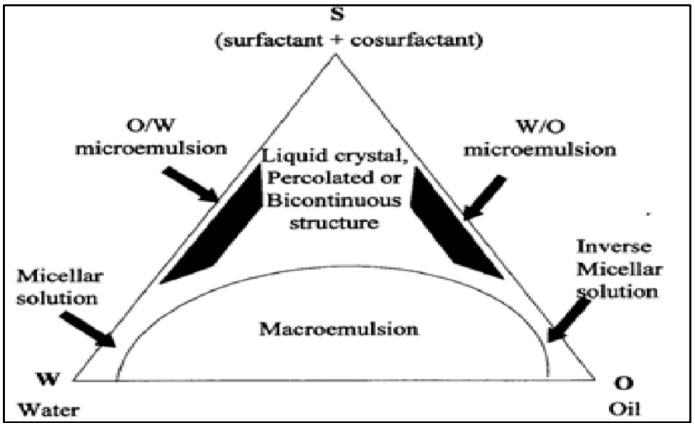

Figure 3: Pseudo-ternary phase diagram

Material and Methods of microemulsion

Phase titration method

Phase diagrams, also known as phase titration technique, are useful for representing microemulsions formed through spontaneous emulsification. They provide a means to study the intricate interactions that happen once altered constituents are combined. The phase diagrams help in understanding the formation of microemulsions and various other association structures, such as emulsions, micelles, lamellar phases, hexagonal phases, cubic phases, gels, and oily dispersions. Every component's content and concentrations are key factors in defining the kind of structure that is developed[36]. Analyzing phase equilibrium and delineating phase boundaries are important aspects of this investigation. Constructing a quaternary phase diagram (four-component system) is time-consuming and challenging towards interoperating. To simplify the process, the pseudo-ternary phase diagram is commonly employed. In this diagram, diverse zones, with the microemulsion zone, can be identified. 100% of every part is shown in each diagram corner. Depending on the presence or absence of water, the region can be categorized as either oil-rich or water-rich microemulsion[37]. When examining these systems, it is important to exercise caution and exclude observations of metastable systems. As the system cools, it passes through a point of minimal surface tension and zero spontaneous curvature, which facilitates the formation of finely dispersed oil droplets. The Phase Inversion Temperature (PIT) method is employed to achieve this. In addition to temperature, other factors such as salt content or pH value may also be considered to determine the microemulsion formation[38].

Phase inversion technique

Phase inversion in microemulsions can occur due to variations in temperature or an excessive amount of the dispersed phase. This transition involves significant physical variations, containing alterations in particle size, which can impact the release of medications both in vitro and in vivo. One approach to induce phase inversion is by modifying the natural curvature of the surfactant. Non-ionic surfactants can achieve this by adjusting the temperature of the system. At low temperatures, an oil-in-water (o/w) microemulsion is formed, while at higher temperatures, water-in-oil (w/o) microemulsion is generated (referred to as transitional phase inversion). During cooling, the system reaches a critical point characterized by minor surface tension and zero spontaneous curvature. This leads to the formation of finely dispersed oil droplets. The Phase Inversion Temperature (PIT) method is employed to facilitate this transition. Temperature is a key variable considered, either in combination with other factors like salt concentration or pH level, or as the sole controlling

factor. Changes in the water volume proportion can also influence the spontaneous radius of curvature. Initially, when water is gradually introduced into the oil, water droplets start to form. As the water volume percentage increases, the spontaneous curvature of the surfactant shifts, resulting in the stabilization of an o/w microemulsion at the phase inversion point, rather than the initial w/o microemulsion. The presence of short-chain surfactants in the o/w interface leads to the formation of flexible monolayers, which contribute to the discontinuous microemulsion that undergoes inversion[39].

The procedure for making micro-emulsion-based gel

1. Making an O/W or W/O microemulsion
2. Formulation of gel base.
3. Stir continuously while incorporating the micro emulsion into the gel foundation.

Evaluation of Microemulsion[40]

- **Viscosity:** To test viscosity, a Brookfield Rotational Viscometer is utilised.
- **pH:** With a digital pH metre, pH is determined**.**
- **Drug Content:** A suitable solvent is used to extract API from a microemulsion that is based on API. The concentration is assessed using a UV-visible spectroscopic technique at its maximal wavelength while maintaining solvent as a reagent blank.
- **Centrifugation:** It is evaluated to determine whether the physical system is stable. A microemulsion is centrifuged at room temperature with 5000 RPM for 10 min to check the system for creaming or phase separation. The visual appeal of the system will be evaluated.
- **Conductivity:** A digital conductometer is used to assess the microemulsion's electric conductivity at room temperature.
- **Dilution Test:** Microemulsion won't be divided into stages if continuous phase is included. Phase separation and purity of the microemulsion will be visually assessed after a 50–100 times continuous phase dilution.
- **% Transmittance Measurement:** With continuous phase, the micro-emulsion will be diluted 50–100 times. A UV-Visible spectrophotometer is used to test the formulation's transmittance at a certain wavelength.
- **Zeta potential and Micelle Size Analysis:** The micelle size, size distribution, and zeta potential of the microemulsion are determined using a particle size analyser.
- **In-vitro release study:** Franz diffusion cells are used for the in-vitro release study.

Characterization of Microemulsion-Based Gel[41, 42]

- **Physical Investigations:** Microemulsion-based gel is examined physically for things like colour, homogeneity, consistency, and texture.
- **pH:** A digital pH metre is used to determine the pH of the manufactured microemulsion-based gels' 1% aqueous solution.
- **Spreadability Dimension:** Spreadability is measured by depositing 0.5 g of microemulsion-based gel within a 1 cm diameter circle that has been pre-marked on a glass plate, which is then covered by a second plate to measure spreadability. The weight of five grams is allowed to rest on the upper glass plate for five minutes. The increase in diameter caused by the microemulsion-based gel spreading is measured in cm/gm-sec.
- **Syneresis measurement test:** When standing, the gel system may occasionally contract slightly and release a little amount of liquid. Syneresis is the name given to this phenomenon. This test uses a perforated plastic tube with a microemulsion-based gel within that is wrapped in filter paper (Whatman No. 41). After that, these tubes will be centrifuged for 15 minutes in tubes. The liquid that was separated from the microemulsion-based gel and the cylindrical plastic tube are weighed. Next, the proportion of syneresis is determined as follows:

$$\% \text{ of Syneresis} = \frac{\text{Weight of Liquid seperated from microemulsion based gel}}{\text{Total weight of microemulsion based gel befoe centrifugation}} \times 100$$

- **Rheological study:** Primarily, the Brookfield Viscometer is used to measure viscosity at 37°C.
- **Drug content determination**: In particular, if you're planning to be traveling a lot, it's an excellent concept to have a backup plan in place. After a suitable dilution, absorbance at maximum nm is measured with a UV spectrophotometer.
- **Tube Test (Extrudability Test):** To assess the extrudability of a microemulsion-based gel formulation, the force needed towards extruding material from the tube must be measured.
- **In-vitro release study:** Franz diffusion cells are used for the in-vitro release study.
- **A drug release kinetics investigation:** The outcomes of the in-vitro release profiles collected for every batch are displayed as
  - Zero order kinetic models – % CPR Vs time.
  - First order kinetic model – log % cumulative drug remaining Vs time.
  - Higuchi's model – % cumulative drug released vs. square root of time.
  - Korsmeyer/Peppa's model – log % cumulative drug released Vs log time.

- Hixson Crowell model – Cube root of % drug to be remaining Vs Time.

- **Skin Irritation:** It is done on a rabbit utilising the Draize-patch test.
- **In-vivo investigation:** the study of animals. Gel based on microemulsions is optimised.
- **Accelerated Stability investigation of a gel based on an improved microemulsion:** An ampoule containing a sample of a microemulsion-based gel that has been loaded with API is sealed, and the ampoule is then placed in an accelerated stability chamber with a temperature of 40ºC±5ºC and a relative humidity of 70%±5%. At 1, 2, and 3 months, duplicate samples are removed in order to assessing their physicochemical characteristics. Visual examination is used to assess the physical stability for physical changes such phase separation and medication precipitation. The amount of medication assessed by UV-Visible spectroscopic technique at max nm is used to represent chemical stability.

Application of Microemulsion Based Gel[43]

Category	Active ingredients	Application
Antifungal	Fluconazole, Voriconazole, Miconazole	Reduce fungal infection around the skin
Antiviral	Penciclovir	Treatment of herpes labialis infection.
Anti-inflammatory	Ibuprofen Ketoprofen	In initial stage of inflammatory symptoms
Antibiotic	metronidazole	Reduce the bacterial infection and improve healing
Antioxidant	Quercetin	Used in anti-aging and cosmetic products

Figure 5: Application of Microemulsion Based Gel

Marketed product of Emulgel

Product Name	Drug	Manufacturer	Use
Voltarol 1.16% emulgel	Diethylammonium {-o-[2,6 dichlorophenyl)-amino]-phenyl}- acetate	Novartis	Anti-inflammatory
DiclomaxEmulgel	Diclofenac sodium	Torrent Pharma	Anti-inflammatory
Miconaz-H-emulgel	Miconazole nitrate, Hydrocortisone	Medical union Pharmaceuticals	Topical corticosteroid and antifungal
Avindo gel	Azithromycin	CosmePharma Laboratories	Antibiotic

Figure 6: Marketed Formulations

Patents of microemulsion based gel

Sr. No.	Patent Application Number	Title of Patent
1	US 2005/0079228 A1	Clear, stable topical compositions of Clarithromycin and Processes for their preparation.
2	US 2005/0037030 A1	Stable topical formulation of Clarithromycin
3	US 8,968,775 B2	Microemulsion topical delivery platform
4	EP 1 588 697 A1	Emulsion gel for topical application of pharmaceuticals
5	US 7,064,114 B2	Gel-Microemulsion Formulations

Figure 7: List of Patents

Conclusion

Topical medication delivery systems have gained widespread use in recent years due to improved patient compliance. Among these systems, emulgels have emerged as highly effective for delivering hydrophobic medications and also as a promising approach for combining hydrophilic and hydrophobic medications. Emulgels provide a means to regulate the release rates of drugs with short half-lives by leveraging the advantages offered by microemulsions and gels in a single formulation. While the number of commercially available microemulsion-based gel formulations is currently limited, there exists significant potential for research and development in this area. Emulgels offer numerous benefits and hold promise for various future applications in derma care. They are advantageous because they contain fewer excessively oily bases and excipients, resulting in enhanced efficacy of the medication.

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References

1. Kasar S. Micro-Emulgel Technique: A Novel Approach for Topical Delivery of Drug. Systematic Review Pharmacy. 2022;13(7):451-456. DOI: 10.31858/0975-8453.13.7.451-456
2. Kushwah P, Sharma PK, Koka SS et al. Microemulgel: a novel approach for topical drug delivery. Journal of Applied Pharmaceutical Research. 2021 Sep 30;9(3):14-20. DOI: 10.18231/j.joapr.2021.v9.i3.14-20

3. Mehta J, Shah CN, Upadhyay UM. Novel Topical Drug Delivery System: Microemulgel-A Review. Research Journal of Pharmaceutical Dosage Forms and Tech.2022; 14(2):171-176.DOI: 10.52711/0975-4377.2022.00027
4. Ashara KC, Paun JS, Soniwala MM et al. Microemulgel: An overwhelming approach to improve therapeutic action of drug moiety. Saudi Pharmaceutical Journal. 2016 Jul 1;24(4):452-7. https://doi.org/10.1016/j.jsps.2014.08.002
5. Singla V, Saini S, Joshi B, Rana AC. Emulgel: A new platform for topical drug delivery. International Journal of Pharma and Bio Sciences. 2012;3(1):485-98.
6. Grampurohit N, Ravikumar P, Mallya R. Microemulsions for topical use–a review. Ind J Pharm Edu Res. 2011 Jan;45(1):100-7.
7. Ramteke KH, Dhole SN, Patil SV. Transdermal drug delivery system: a review. Journal of Advanced Scientific Research. 2012 Feb 10;3(01):22-35. https://sciensage.info/index.php/JASR/article/view/72
8. Bhowmik D. Recent advances in novel topical drug delivery system. The Pharma Innovation. 2012 Nov 1;1(9);12-31.
9. Tanwar H, Sachdeva R. Transdermal drug delivery system: A review. International journal of pharmaceutical sciences and research. 2016 Jun 1;7(6):2274-2290. DOI: 10.13040/IJPSR.0975-8232.7(6).2274-90
10. Arunachalam A, Karthikeyan M, Kumar DV et al. Transdermal drug delivery system: a review. Journal of Current Pharma Research. 2010 Oct 1;1(1):70.
11. Jeong WY, Kwon M, Choi HE et al. Recent advances in transdermal drug delivery systems: A review. Biomater Research. 2021;25:1-5.
12. Chillistone S, Hardman JG. Factors affecting drug absorption and distribution. Anaesthesia & Intensive Care Medicine. 2017 Jul 1;18(7):335-9. https://doi.org/10.1016/j.mpaic.2017.04.007
13. Singh I, Morris AP. Performance of transdermal therapeutic systems: Effects of biological factors. International journal of pharmaceutical investigation. 2011 Jan;1(1):4-9. https://doi.org/10.4103%2F2230-973X.76721
14. Mali AD. An updated review on transdermal drug delivery systems. skin. 2015;8(9);244-254. DOI: 10.7439/ijasr
15. Nicol NH. Anatomy and physiology of the skin. Dermatology nursing. 2005 Feb 1;17(1):62-3.
16. Dehdashtian A, Stringer TP, Warren AJ et al. Anatomy and Physiology of the Skin. In Melanoma: A Modern Multidisciplinary Approach. Springer International Publishing.

2018;15–26. doi: 10.1007/978-3-319-78310-9_2

17. McLafferty E, Hendry C, Farley A. The integumentary system: anatomy, physiology and function of skin. Nursing Standard (through 2013). 2012 Sep 19;27(3):35-42.
18. Kolarsick PA, Kolarsick MA, Goodwin C. Anatomy and physiology of the skin. Journal of the Dermatology Nurses' Association. 2011 Jul 1;3(4):203-13. *DOI:* 10.1097/JDN.0b013e3182274a98
19. Montagna W. Comparative anatomy and physiology of the skin. Arch Dermatology. 1967;96(4):357–63. https://pubmed.ncbi.nlm.nih.gov/4862694/
20. Gaboriau HP, Murakami CS. Skin anatomy and flap physiology. Otolaryngologic Clinics of North America. 2001 Jun 1;34(3):555-69.DOI:https://doi.org/10.1016/S0030-6665(05)70005-0
21. Shingade GM. Review on: recent trend on transdermal drug delivery system. Journal of drug delivery and therapeutics. 2012 Jan 19;2(1):66-75. DOI https://doi.org/10.22270/jddt.v2i1.74
22. Das A, Ahmed AB. Natural permeation enhancer for transdermal drug delivery system and permeation evaluation: A review. Asian J Pharm Clin Res. 2017;10(9):5-9. DOI: http://dx.doi.org/10.22159/ajpcr.2017.v10i9.19389
23. Rastogi V, Yadav P. Transdermal drug delivery system: An overview. Asian Journal of Pharmaceutics (AJP). 2012;6(3):161-170. DOI: https://doi.org/10.22377/ajp.v6i3.51
24. Jhawat VC, Saini V, Kamboj S et al. Transdermal drug delivery systems: approaches and advancements in drug absorption through skin. Int J Pharm Sci Rev Res. 2013 May;20(1):47-56.
25. Lawrence MJ, Rees GD. Microemulsion-based media as novel drug delivery systems. Advanced drug delivery reviews. 2012 Dec 1;64:175-93. https://doi.org/10.1016/j.addr.2012.09.018
26. Dev A, Chodankar R, Shelke O. Emulgels: a novel topical drug delivery system. Pharmaceutical and biological evaluations. 2015 Aug 26;2(4):64-75.
27. Patel K, Patel R, Patel M. Formulation and characterization of microemulsion based gel of antifungal drug. PharmaTutor. 2014 Feb 1;2(2):79-89.
28. Howe AM, Katsikides A, Robinson BH, Chadwick AV, Al-Mudaris A. Structure and dynamics of microemulsion-based gels. Trends in Colloid and Interface Science II. 1988:211-5. https://link.springer.com/chapter/10.1007/BFb0114194
29. Patel RR, Patel ZK, Patel KR et al. Micro emulsion based gel: recent expansions for topical drug delivery system. Journal of medical pharmaceutical and allied sciences.

2014;1:1-5.

30. Kale SN, Deore SL. Emulsion micro emulsion and nano emulsion: a review. Systematic Reviews in Pharmacy. 2017;8(1):39-47. DOI : 10.5530/srp.2017.1.8
31. Madhav S, Gupta D. A review on microemulsion based system. International Journal of Pharmaceutical Sciences and Research. 2011 Aug 1;2(8):1888-99.
32. Patel A, Patel J. Mucoadhesive microemulsion based prolonged release vaginal gel for anti-fungal drug. American Journal of Pharma Technology and Research. 2012;2(4):650-61.
33. Chandra A, Sharma PK, Irchhiaya R. Microemulsion-based hydrogel formulation for transdermal delivery of dexamethasone. Asian Journal of Pharmaceutics (AJP). 2009;3(1):30-36. DOI: https://doi.org/10.22377/ajp.v3i1.238
34. Trickett K, Eastoe J. Surfactant-based gels. Advances in colloid and interface science. 2008 Dec 2;144(1-2):66-74. https://doi.org/10.1016/j.cis.2008.08.009
35. Abd Sisak MA, Daik R, Ramli S. Study on the effect of oil phase and co-surfactant on microemulsion systems. Malaysian Journal of Analytical Sciences. 2017;21:1409-16. DOI: https://doi.org/10.17576/mjas-2017-2106-23
36. Sujatha B, Himabindu E, Abbulu K et al. Microemulsions-A review. Journal of Pharmaceutical Sciences and Research. 2020 Jun 1;12(6):750-3.
37. Konyakhina TM, Wu J, Mastroianni JD et al. Phase diagram of a 4-component lipid mixture: DSPC/DOPC/POPC/chol. Biochimica et Biophysica Acta (BBA)-Biomembranes. 2013 Sep 1;1828(9):2204-14. https://doi.org/10.1016/j.bbamem.2013.05.020
38. Yadav V, Jadhav P, Kanase K et al. Preparation and evaluation of microemulsion containing antihypertensive drug. International Journal of Applied Pharmaceutics. 2018 Sep 7;10(5):138-46. DOI: http://dx.doi.org/10.22159/ijap.2018v10i5.27415
39. Fernandez P, André V, Rieger J et al. Nano-emulsion formation by emulsion phase inversion. Colloids and Surfaces A: Physicochemical and Engineering Aspects. 2004 Dec 20;251(1-3):53-8. https://doi.org/10.1016/j.colsurfa.2004.09.029
40. Shinde U, Pokharkar S, Modani S. Design and evaluation of microemulsion gel system of nadifloxacin. Indian journal of pharmaceutical sciences. 2012 May;74(3):237-47. doi: 10.4103/0250-474X.106066.
41. Nikumbh KV, Sevankar SG, Patil MP. Formulation development, in vitro and in vivo evaluation of microemulsion-based gel loaded with ketoprofen. Drug delivery. 2015 May 19;22(4):509-15. https://doi.org/10.3109/10717544.2013.859186

42. Sabale V, Vora S. Formulation and evaluation of microemulsion-based hydrogel for topical delivery. International journal of pharmaceutical investigation. 2012 Jul;2(3):140-49. doi: 10.4103/2230-973X.104397

43. Boonme P, Kaewbanjong J, Amnuaikit T et al. Microemulsion and microemulsion-based gels for topical antifungal therapy with phytochemicals. Current pharmaceutical design. 2016 Aug 1;22(27):4257-63.