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Comprehensive Review on Emulgel as a Novel Drug Delivery System for Topical Application.

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Abstract: *Emulgel represents an innovative advancement in topical drug delivery, merging the advantages of both gels and emulsions to effectively deliver hydrophilic as well as lipophilic drugs. This hybrid system overcomes many drawbacks of conventional topical dosage forms such as ointments and creams by improving drug stability, spreadability, and patient compliance. Incorporation of a gelling agent in the aqueous phase transforms a standard emulsion into an emulgel. These formulations, which can be either oil-in-water or water-in-oil emulsions, play a significant role in treating various conditions, including poisoning, inflammation, fungal infections, and acne. By combining the characteristics of an emulsion and a gel, emulgels enhance the solubility of poorly soluble drugs and offer several desirable properties such as thixotropy, non-greasiness, easy washability, emollient nature, transparency, longer shelf life, and good aesthetic appeal. These qualities make emulgels particularly suitable for dermatological and transdermal drug delivery. This review highlights the formulation strategies, components, advantages, and evaluation parameters of emulgels, along with recent developments in both herbal and pharmaceutical emulgel applications for skin therapy*

Keywords: Emulgel, Topical drug delivery, Gelling agents, Hydrophobic drugs, Dermatological formulation

I. INTRODUCTION

Topical drug therapy has been practiced since ancient times for treating dermatological and cosmetic conditions. A wide range of active agents such as anti-inflammatory, antibacterial, antifungal, antiviral, anti-acne, antipigmentary, and emollient compounds can be directly applied to the skin [1]. The key benefit of topical delivery lies in its ability to provide localized drug action while avoiding hepatic first-pass metabolism[2].

For a drug to act effectively, however, it must penetrate the skin through multiple layers to reach its target site. Topical systems also eliminate challenges associated with oral and intravenous routes, such as pH variation, enzymatic degradation, and gastric emptying time [2]. The release rate of drugs from topical formulations largely depends on the physicochemical properties of both the drug and the carrier vehicle.

Semisolid preparations (such as creams, gels, and ointments) are the most commonly used topical dosage forms. Among these, emulgels have gained popularity because of their ability to combine the properties of gels and emulsions. A typical emulgel is formed when a gelling agent is incorporated into the aqueous phase of an emulsion, improving its viscosity, stability, and spreadability [3]. Hydrophilic drugs are retained within the aqueous phase of W/O systems, whereas lipophilic drugs are dispersed in the oil phase of O/W systems [4].

Within the semisolid class, clear or translucent gels are increasingly used in pharmaceutical and cosmetic products. Gels consist of a network of polymeric or colloidal solid particles capable of trapping large volumes of aqueous or hydroalcoholic liquids. They offer faster drug release than creams or ointments. However, their limitation lies in delivering poorly soluble or hydrophobic drugs [5].

Topical formulations can be designed for local or systemic therapeutic effects, depending on drug properties and formulation design. Drug penetration through the skin depends on molecular size, solubility, and lipid water partition coefficient. Ideally, a topical preparation should provide prolonged local contact with minimal systemic absorption [6].

The skin, covering approximately 1.7 m² and constituting nearly 10% of total body weight, acts as a primary protective barrier and an efficient route for drug absorption. Because of its structural complexity and absorptive capacity, the skin has become a preferred site for localized and controlled drug delivery [7].

Solid Preparation	Liquid preparation	Semisolid preparation	Miscellaneous preparation
Topical powder	Lotion	Ointment	Transdermal drug delivery system
Poultices	Liniment	Creams	Tapes and Gauzes
Plaster	Paints	Pastes	Rubbing Alcohols liquid cleaner
	Solution	Gel	Topical aerosol
	Emulsion	Suppository	
	Suspension		

Table 1: Classification of topical drug delivery system [3]

• Advantages of topical drug delivery system

1. Steer clear of first pass metabolism.
2. The capability to quickly stop taking the drugs as necessary.
3. The capacity to administer a medication more precisely to a particular location.
4. Preventing gastrointestinal incompatibility.
5. Easy to use and convenient [8].

• Disadvantages of topical drug delivery system

1. Certain drugs have poor skin permeability.
2. Secondly, contact dermatitis causes skin irritation.
3. Drugs with big particles are difficult for the skin to absorb.
4. A potential allergic response [8] .

Physiology of Skin [9]

Since most topical formulations are designed for application directly onto the skin, a thorough understanding of the skin's physiology and functional characteristics is essential in developing effective topical drug delivery systems. In an average adult, the skin covers approximately 2 square meters of surface area and receives nearly one-third of the total blood circulation in the body. On average, each square centimeter of the skin contains 40– 70 hair follicles and about 200–300 sweat glands. The pH of the skin generally ranges from
4.0 to 5.6, making its surface slightly acidic. This acidity is primarily maintained by the secretion of sweat and the release of fatty acids from sebaceous glands, both of which contribute to maintaining the skin's protective barrier. Anatomically, the skin is composed of four distinct layers of tissue, as illustrated in Figure (refer to figure section), each performing specific structural and physiological roles vital to topical absorption and protection of the body.

1. Epidermis
2. Dermis
3. Subcutaneous connective tissue

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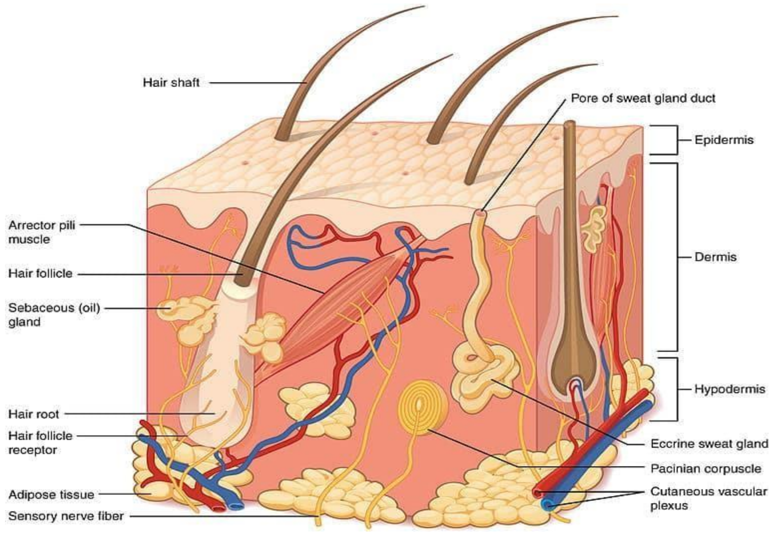

Fig 1: Physiology of Skin [13].

1. Epidermis

The skin's outermost layer, the epidermis, is where substances applied topically come into direct contact with the skin. It is composed of stratified squamous epithelial cells and lacks blood vessels, acting mainly as a barrier for protection.
The five layers that make up the epidermis are as follows:
Stratum Corneum: With 20–30 cells, this is the thickest and outermost layer. Lucidum Stratum
Stratum Spinosum Granulosum
Stratum Basale: The epidermis's deepest layer[11].

2. Dermis

Situated directly beneath the epidermis, the dermis serves as the structural foundation of the skin. It is composed primarily of loose connective tissue and measures about 2000– 3000 µm in thickness. This layer provides mechanical support, elasticity, and nourishment to the epidermis. The dermis is divided into two main regions: the papillary layer and the reticular layer. Both layers contain vital structural proteins such as collagen, elastin, and fibrillin, which together maintain the skin's strength and elasticity. The dermis also houses important anatomical components, including hair follicles, sweat glands, sebaceous glands, blood vessels, and sensory nerve endings. These structures regulate temperature, sebum secretion, and sensory perception. Moreover, the network of capillaries within the dermis supplies the epidermis with oxygen and essential nutrients, ensuring tissue vitality and resilience [10].

3. Subcutaneous Connective Tissue

The subcutaneous tissue, also known as the hypodermis, lies beneath the dermis and is composed mainly of loosely arranged white fibrous connective tissue interspersed with fat cells, cutaneous nerves, sweat gland ducts, and blood and lymphatic vessels. Although it plays a significant role in insulation, cushioning, and energy storage, it is often not considered a true part of the skin's organized connective tissue.The fatty matrix of the hypodermis can function as a drug reservoir, allowing slow diffusion of certain compounds. However, most topical drugs enter systemic circulation before reaching this layer, as the hypodermis is generally located beyond the main barrier of transdermal absorption [12,42].

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Factors Affecting Topical Absorption of Drug

1. Physiological Factors

• Skin thickness.
• Lipid content.
• Density of hair follicles.
• Density of sweat glands.
• Skin pH.
• Blood flow.
• Hydration of skin.

2. Physiochemical Factors

• Partition coefficient.
• Molecular weight (<400 Dalton).
• Degree of ionization (only unionized drugs gets absorbed well).
• Effect of vehicles.
• Diffusion coefficient.
• Permeability coefficient. [14]

Method to Enhance Drug Penetration and Absorption

1. Chemical enhancement
2. Biochemical enhancement
3. Physical enhancement
4. Super saturation enhancement[15]

Rationale of Emulgel as a Topical Drug Delivery System

Topical or dermatological formulations are designed to be applied directly onto the skin or mucous membranes with the aim of restoring normal skin function or producing a localized pharmacological effect in the underlying tissues. While conventional topical dosage forms such as creams, ointments, and lotions are widely used, they often suffer from several limitations. Their greasy and sticky nature can lead to patient discomfort, poor aesthetic appeal, and reduced compliance [16]. Among semisolid formulations, gels offer multiple advantages such as excellent spreadability, rapid drug release, non-greasiness, ease of removal, and thixotropic behavior. However, a major limitation of gels is their inability to effectively deliver hydrophobic drugs, as these drugs exhibit poor solubility in the aqueous medium typically used in gel bases. Consequently, drug diffusion and skin penetration are restricted unless solubility enhancers or penetration promoters are incorporated [17].Structurally, gels are colloidal systems containing up to 99% liquid phase, which is immobilized within a network of macromolecular polymers. Despite their favorable properties, the challenge of incorporating lipophilic or poorly water-soluble drugs remains significant [16].To overcome this drawback, the concept of the emulgel was developed. Emulgels combine the principles of emulsion and gel technologies, allowing the successful encapsulation and delivery of hydrophobic drugs within a stable, patient-friendly, and aesthetically acceptable formulation. This dual system enhances both drug solubility and skin penetration, making it a promising and effective approach for topical drug delivery
[17].

Emulsion

An emulsion is a biphasic liquid dosage form composed of two immiscible liquids typically oil and water in which one phase (the dispersed phase) is finely distributed as small droplets within the other (the continuous phase). Because oil

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and water are inherently immiscible, emulsions are thermodynamically unstable systems and require the addition of emulsifying agents (surfactants) to maintain stability [18].

Gel

The term "gel" refers to a semisolid system in which a gelling agent increases the viscosity of a liquid preparation without altering its fundamental properties. Gels are often utilized as thickening agents to enhance the uniformity, stability, and consistency of pharmaceutical formulations. In emulgel preparation, a gel base is first developed and then combined with an emulsion to form the final product. Gels consist of polymeric networks that swell upon contact with a solvent, often entrapping significant amounts of liquid within their three- dimensional structure. The rigidity or firmness of the gel depends on the volume of liquid retained and the cross-linking density of the polymer matrix. Such properties make gels highly suitable for topical drug delivery applications [19,14].

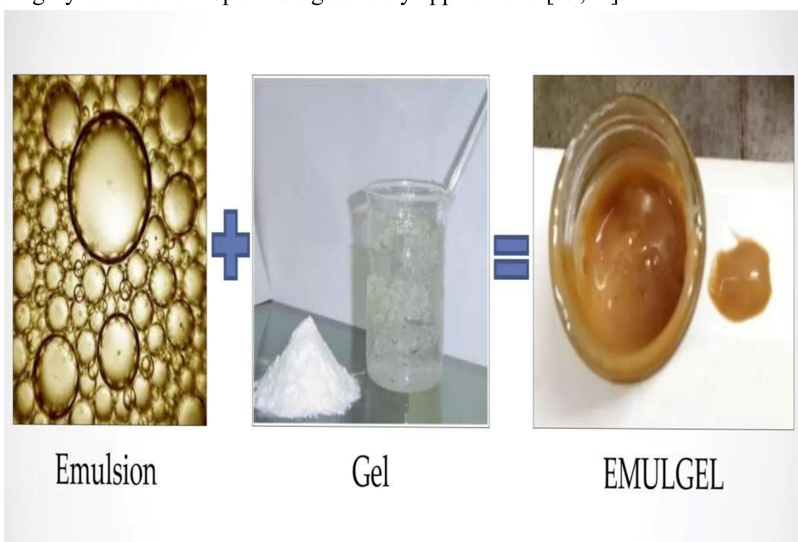

Fig 2: Emulsion + Gel= Emulgel [20]

Emulgel

An emulgel is a hybrid topical formulation that integrates the properties of both emulsions and gels. It is essentially an oil-in-water (O/W) or water-in-oil (W/O) emulsion that is incorporated into a gelling matrix to obtain a stable semisolid system. By combining these two dosage forms, emulgels overcome many limitations of conventional gels and emulsions, offering improved stability, spreadability, and drug penetration . The process of transforming an emulsion into a gel enhances its viscosity and structural integrity, resulting in better therapeutic performance compared to ordinary gels. Moreover, emulgels provide a dual-controlled release mechanism the gel network regulates drug diffusion, while the emulsion phase controls drug partitioning between the oil and aqueous layer..[21] The type and concentration of the gelling polymer play a critical role in determining the stability, rheology, and drug release rate of the final formulation. Due to their mucoadhesive characteristics, emulgels can maintain prolonged contact with the skin, ensuring sustained drug delivery at the application site.[24] Additionally, emulgels can serve as an effective alternative to oral and parenteral routes by avoiding issues such as first-pass metabolism, absorption variability, and the inconvenience or risks associated with intravenous administration, making them a versatile and patient-friendly delivery system [21].

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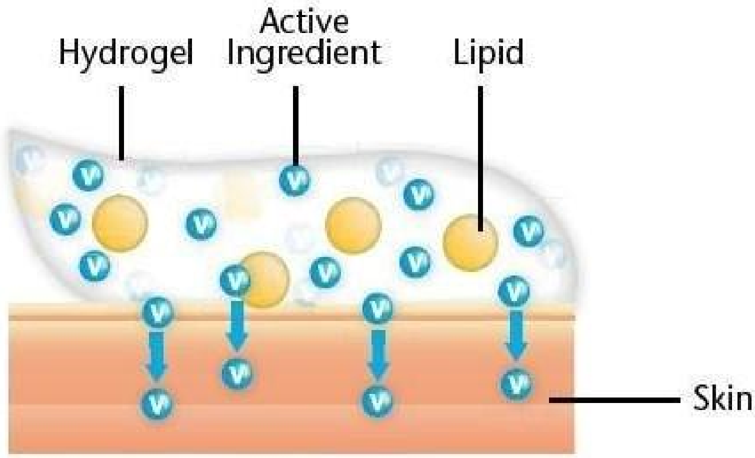

Fig 3: Emulgel [22]

Fig 4: Advantages of Emulgel [23]

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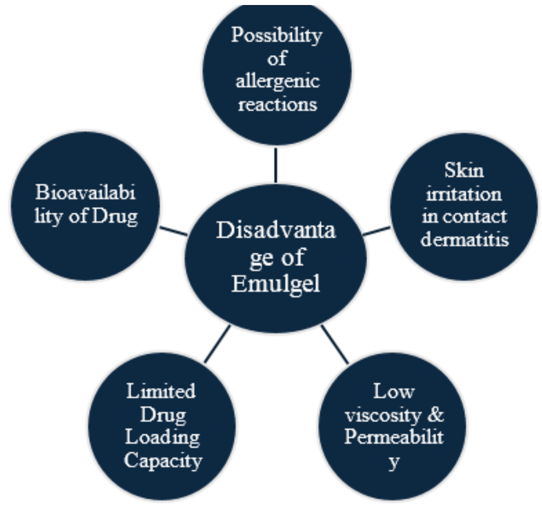

Fig 5 : Disadvantages of Emulgel [23]

Properties of emulgel

1. Thixotropic:

Emulgels exhibit thixotropic behavior, meaning they can easily transition from a semi-solid gel to a liquid state when subjected to shear stress (such as rubbing) and revert to their original form upon standing. This property ensures smooth application and even spreading over the skin surface.

2. Greaseless:

Unlike conventional ointments, emulgels are non-greasy and do not leave an oily residue after application. This enhances patient compliance and makes them more cosmetically appealing.

3. Easily Washable:

Emulgels can be readily removed with water, offering better cleanability and convenience compared to oil-based formulations.

4. Emollient Effect:

These formulations possess moisturizing properties, helping to maintain skin hydration and softness, which supports overall skin health.

5. Non-Staining:

Emulgels typically do not stain clothes or surfaces, as they are free from heavy oils and pigments, making them aesthetically favorable for users.

6. Extended Shelf Life:

Due to their physicochemical stability, emulgels generally have a longer shelf life, maintaining their consistency, appearance, and efficacy over time[24,46].

Classification of Emulgel

1. Based on Nature of Active Ingredient

a) Herbal / Polyherbal Emulgel

Herbal and polyherbal emulgels are formulated using plant-derived ingredients or combinations of herbal extracts for therapeutic or cosmetic applications. Examples include:

• Cosmetic Emulgel prepared from field pumpkin for skin nourishment and care.

• Anti-psoriatic Emulgel formulated using babchi oil and Gum Guggul, both known for their potent anti-inflammatory and skin-rejuvenating properties.

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b) Allopathic Emulgel

Allopathic emulgels incorporate synthetic drugs in a gel-based emulsion for targeted delivery and enhanced skin absorption. Example: Diclofenac diethylammonium Emulgel (Voltaren®), developed by Novartis Pharma, is a well-known formulation used for local pain and inflammation relief [25].

2. Based on Type of Emulsion

a) Macroemulsion Gel

Macroemulsion based emulgels are the most common type, consisting of emulsion droplets larger than 400 nm in diameter. Although invisible to the naked eye, these droplets can be clearly observed under a microscope. Macroemulsions are thermodynamically unstable, but their stability can be enhanced by incorporating surface-active agents (surfactants) that reduce interfacial tension and prevent phase separation [26].

b) Microemulsion Gel

Microemulsion gels are optically transparent, thermodynamically stable, and consist of an isotropic mixture of oil and water stabilized by surfactants and co-surfactants. The droplet size ranges between 10 and 100 nm, allowing for efficient solubilization of both hydrophilic and lipophilic drugs. Their unique properties include a large interfacial surface area, low interfacial tension, and enhanced permeability through the skin. Microemulsion components can facilitate drug penetration by reducing the diffusion resistance of the stratum corneum. However, their low viscosity and limited skin retention often restrict their practical use in topical formulations [27].

c) Nanoemulsion Gel

When nanoemulsions are incorporated into a gel base, the resulting formulation is called a nanoemulgel. These systems are characterized by droplet sizes below 100 nm, producing transparent or translucent dispersions stabilized by surfactant and co-surfactant layers at the oil water interface. Nanoemulgels exhibit high thermodynamic stability, improved drug loading, and enhanced transdermal permeation compared to conventional gels and emulsions. Both in vitro and in vivo studies have demonstrated that nanoemulgels significantly improve dermal and transdermal drug delivery, making them a promising platform for future topical therapeutics [28].

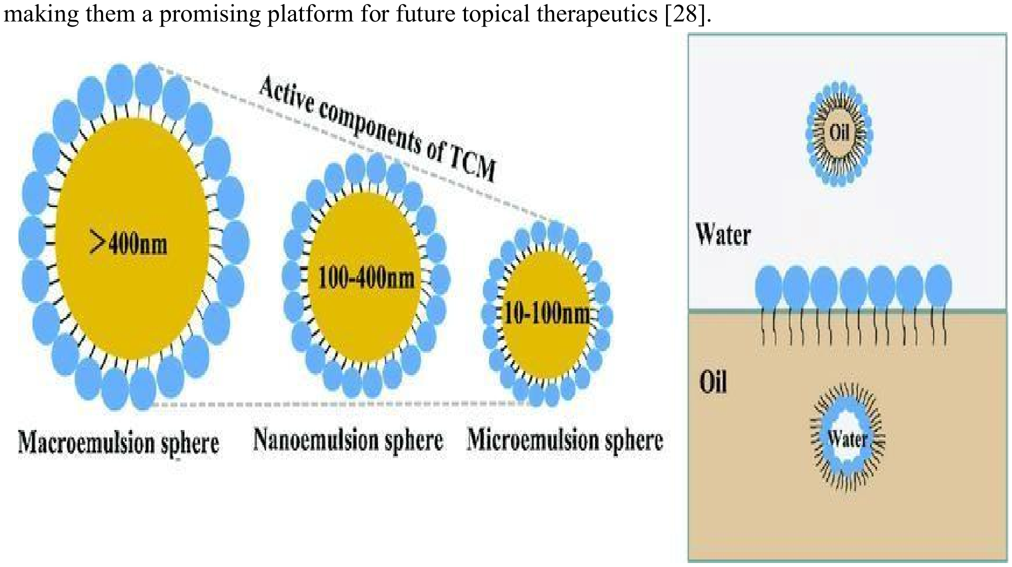

Fig 6: Types of Emulgels [29]

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Components of Emulgel

1. Aqueous Material

The aqueous phase forms the continuous portion of the emulsion system and serves as the medium for hydrophilic ingredients. Commonly used aqueous materials include purified water and alcohols, which help dissolve water-soluble components and maintain the desired consistency of the formulation. The aqueous phase also aids in the dispersion of the gelling agent and enhances the overall stability of the emulgel[30].

2. Oils

The oil phase constitutes the dispersed part of the emulsion and plays a key role in drug solubilization. Mineral oils, either alone or in combination with soft or hard paraffins, are widely utilized in topical formulations due to their excellent emollient and barrier-forming properties. In addition to mineral oils, non-biodegradable oils such as castor oil and nutritional fixed oils like arachis (peanut), cottonseed, maize, and fish liver oils are frequently used. These oils not only function as vehicles for the drug but also contribute to the texture, spreadability, and stability of the emulsion phase. In oral formulations, such oils may also provide nutritional or therapeutic benefits [31].

Chemical	Quantity	Formulation
Light Liquid Paraffin	7.5%	Emulgel
Isopropylmyristate	7-7.5%	Emulsion
Isopropyl stearate	7-7.5%	Emulsion
Isopropyl palmitate	7-7.5%	Emulsion
Propylene glycol	3.5%	Gel

Table 2: Quantity of oils to be used in preparation of emulsion[39]

3. Emulsifiers

Emulsifiers play a vital role in reducing interfacial tension between immiscible liquids, thereby promoting the formation and stabilization of emulsions. The choice of emulsifier depends on its Hydrophilic Lipophilic Balance (HLB) value. In general, surfactants with HLB values greater than 8 are suitable for oil-in-water (O/W) emulsions, while those with HLB values less than 8 are ideal for water-in-oil (W/O) systems. Commonly used emulsifiers include both hydrophilic and lipophilic surfactants. For example, Spans (such as sorbitan monooleate, span 80) are preferred for the oil phase, whereas Tweens (such as polyoxyethylene sorbitan monooleate, Tween 80) are used for the aqueous phase. A combination of Span and Tween often provides superior stability compared to individual use[32,43].

4. Gelling Agents

Gelling agents are essential components that transform the liquid phase of an emulsion into a semi-solid gel structure, forming the base of an emulgel. Also referred to as thickening agents, they increase the viscosity of the formulation by swelling in the aqueous phase, creating a gel- like matrix that enhances drug stability and controlled release[40]. Incorporation of an appropriate gelling agent imparts thixotropic behavior to the system, improving its spreadability and user acceptability. Among various gelling materials, Hydroxypropyl Methylcellulose (HPMC)-based emulgels have shown superior drug release profiles compared to Carbopol-based formulations. Similarly, Sodium Carboxymethyl Cellulose (NaCMC)-based emulgels are preferred for vaginal applications due to their high mucoadhesive strength, which prolongs drug residence time and enhances both in-vitro and in-vivo performance.On the other hand, Hydroxyethyl Cellulose (HEC)-based emulgels provide good drug release and rheological properties but exhibit lower mucoadhesion[44]

Gelling agents	Active pharmaceutical ingredient
Sodium CMC	Benzydamine
Carbopol – 934	Chlorphenesin
Carbopol-940	Mefenamic acid

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HPMC	Clorphenesin

5. Permeation/penetration enhancers

Permeation enhancers, also referred to as penetration enhancers, are substances that temporarily and reversibly increase the permeability of the skin, thereby facilitating the transdermal transport of drugs[45]. These agents work by interacting with the structural components of the stratum corneum and modifying its barrier properties. Their mechanisms of action may include altering the partitioning behavior of drugs within skin layers, disrupting lipid organization, or fluidizing the lipid bilayers present between corneocytes. As a result, the drug can more easily diffuse through the skin and reach the target site. Commonly used natural penetration enhancers include menthol and clove oil, both of which are known to effectively enhance drug absorption without causing permanent skin damage [34].

Permeation Enhancer	Quantity	Dosage Form
Oleic acid	1%	Gel
Mentha oil	6%	Emulgel
Clove oil	10%	Emulgel
Olive oil	6%	Gel
Oleic acid	10%	Gel
Propylene glycol	10%	Gel
Tween 80	5%	Gel
Brij 92	0.5%	Emulgel

Table 4: Examples of Permeation enhancers [35]

• Properties of Penetration Enhancers

o They must be non-toxic, non-irritating, and non-sensitizing, ensuring that they do not cause any allergic or inflammatory reactions upon skin application.

o These agents should be pharmacologically inert, meaning they do not interact with biological receptors or interfere with the therapeutic activity of the incorporated drug.

o Their onset, intensity, and duration of action should be predictable and reproducible, allowing consistent drug permeation through the skin.

o They should exhibit good skin compatibility and cosmetic acceptability, maintaining the integrity and natural appearance of the skin surface.

o Penetration enhancers must be chemically and physically compatible with both active pharmaceutical ingredients (APIs) and formulation excipients.

o Importantly, these substances should facilitate the permeation of therapeutic agents only, without disrupting the normal physiological balance or allowing the loss of endogenous substances from the body [36].

• Mechanism of Penetration Enhancers [37]

Penetration enhancers improve drug absorption through the skin by acting via one or more of the following mechanisms:

1. Disruption of the Stratum Corneum Lipid Structure:

These agents can alter the highly ordered lipid arrangement in the stratum corneum, increasing lipid fluidity and thereby enhancing drug diffusion.

2. Interaction with Intercellular Proteins:

Some enhancers interact with the protein components of the skin, leading to changes in their structural conformation or inducing solvent swelling, which increases the porosity of the stratum corneum.

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3. Improved Drug Partitioning:
Penetration enhancers may improve the partitioning of the drug, solvent, or co-enhancer into the skin layers, allowing for better absorption.
Certain fatty acid–based enhancers increase the fluidity of both lipid and protein regions within the stratum corneum. Some modify the multilamellar lipid pathway, thereby influencing both polar and non-polar diffusion routes. Overall, the mechanism of enhancement and the extent of absorption depend on the chemical nature and concentration of the enhancer employed. The selection of an appropriate enhancer is a key step in formulation design and development [37].

Marketed Formulations

Drug	Marketed product	Manufacturer
Diclofenac sodium	Pennsaid	Nuva Pharma
Aceclofenac	Acent gel	Intas Labs India Pvt. Ltd
Diclofenac-diethyl- ammonium	Voltaren emulgel	Novartis Pharm
Clindamycin phosphate, Allantoin	Clingel	Stiefel Pharma
Clindamycin, Adapalene	Excex gel	Zee Laboratories
Metronidazole, Clindamycin	Lupigyl gel	Lupin Pharma
Benzoyl Peroxide	Pernox gel	Cosme remedies Ltd
Azithromycin	Avindo gel	Cosme Pharma Lab

Table 5: Marketed formulation of Emulgel [47-48]

Recent Research in Emulgel

Drug	Carrier System	Method Used	Uses	Key Results
Dexibuprofen	Carbopol 934 + Propylene glycol	Drug dissolved → emulsion formed → mixed with gel base → evaluated	Anti-inflammatory	Better permeability, high release [49]
Mefenamic Acid	O/W Emulgel using Carbopol	Emulsification + gel base incorporation	Topical anti-inflammatory and analgesic	Improved anti-inflammatory effect, stable[50]
Clotrimazole	Antifungal Emulgel optimized with polymer gelling agent	O/W emulsification + Carbopol gel base	Topical fungal infections	High antifungal activity, ideal rheological properties [51]
Polyherbal Neem-Based (Neem oil + Herbal oils)	Polyherbal Emulgel	Herbal oil emulsification + gelling	Antibacterial, wound healing	antibacterial activity and synergistic herbal effect [52]
Ketoconazole	Emulgel using Carbopol 940	O/W emulsification → gel base	Antifungal infections	Improved permeation & antifungal efficacy[53]
NSAIDs (Diclofenac/Aceclofenac type—NSAID class)	Carbopol 934 gel base + liquid paraffin + Span/Tween emulsifiers	O/W emulsion prepared → mixed into Carbopol gel base with gentle stirring	Antiinflamm atory topical delivery	improved drug release and good spreadability [54]
Clarithromyci n	Carbopol 940 + oil phase Emulsion	incorporation into Carbopol / HPMC	Antibacterial topical therapy	Sustained release, good viscosity [39]

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	prepared → neutralized			
Diclofenac sodium	Carbopol 934/940 + O/W emulsion	O/W emulsion formed → added slowly into gel with continuous homogenization	Anti inflammatory , analgesic	Highest drug release, smooth texture, stable Formulation [55]
Itraconazole	Carbopol + Liquid paraffin	Oil phase + aqueous phase heated → emulsified → blended with gel	Antifungal	Good solubility, uniform release [41]

Table 6: Recent research drug used in Emulgel

II. CONCLUSION

Emulgels have emerged as one of the most promising approaches in topical drug delivery by effectively combining the benefits of both emulsions and gels into a single, stable, and patient-friendly formulation. Their unique dual-release characteristics enable efficient delivery of hydrophobic as well as hydrophilic drugs, ensuring enhanced skin penetration, prolonged retention, and improved therapeutic efficacy. The versatility of emulgels makes them suitable for a wide range of pharmaceutical and cosmetic applications, including anti- inflammatory, antifungal, analgesic, and anti-aging therapies.

Despite their proven potential, challenges such as large-scale manufacturing, physical stability, and regulatory standardization remain key areas requiring further optimization. Future advancements may focus on integrating nanotechnology, stimuli-responsive polymers, and herbal actives to design next-generation "smart emulgels" with targeted, controlled, and patient-specific effects. With continued research and technological innovation, emulgels are poised to play a significant role in modern dermatological and transdermal drug delivery systems.

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