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REVIEW ARTICLE

Exploring emulgel: A comprehensive review on types, ingredients, preparation methods, and characterization approaches

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ABSTRACT

Recent attention has been focused on the utilization of new polymers, which hold significant promise across various applications. The unique significance of dermatological pharmacology stems from the skin's direct accessibility as a target organ for diagnostics and treatment. The skin's unique composition poses challenges for drug delivery, as both hydrophilic and hydrophobic substances encounter barriers formed by the interaction between hydrophilic cornified cells and hydrophobic intercellular material. To address these challenges, emulgel has emerged as a notable solution. Emulgel, a blend of gel and emulsion, presents a promising method for delivering hydrophobic medicines effectively. It offers dual release controls through its gel and emulsion components. It is transparent, facilitating visibility of the application area, and emollient, leaving the skin feeling soft and moisturized. Moreover, emulgel is greaseless, ensuring a non-oily application experience. Its formulation enables easy spreading and detachment from the skin, enhancing usability and adherence. By mixing a surfactant with a co-surfactant, emulgel is a preparation with low interfacial tension and strong thermodynamic stability. It has various features, including enhanced permeability and good thermodynamic stability. The formulation is evaluated for a number of characteristics, including as skin irritancy, medication content, pH, viscosity, particle size, zeta potential, and other pertinent elements.

INTRODUCTION

Localized API distribution anyplace in body via numerous channels is thought to be made easiest and simpler by topical drug administration. There are many different dermatological and cosmetic preparations available for both healthy and tired skin. Emulgels are made by combining gels and emulsions [1], and they are used to administer drugs to the skin using both W/O and O/W emulsions as carriers. They possess a strong ability to effectively enter the skin. An emulgel is created when a standard emulsion has a gelling ingredient in the water phase. Emulgels designed for dermatological purposes boast numerous desirable characteristics [2, 3], including thixotropic properties, greaseless texture, easy spreadability, efficient removal, emollient effects, non-staining properties, water solubility, extended shelf life under realistic conditions of use, biocompatibility, and aesthetically pleasing appearance.

Gel formulations typically offer faster medication release than traditional ointments and lotions. Gels' principal drawback is their incapacity to disperse hydrophobic medications efficiently. Emulgels have been developed to get around this restriction, allowing even hydrophobic medications to benefit from gels' beneficial qualities. Termed as such, emulgel formulations combine emulsions with gels. In essence, an emulgel is created when a gelling ingredient is added to the water phase of a standard emulsion. In emulgels hydrophilic medications is encapsulated within the water-in-oil (W/O) system, while lipophilic drugs are encapsulated within the oil-in-water (O/W) system [4, 5]. As their name implies, emulgels represent a fusion of emulsion and gel. They facilitate the delivery

of various medications to the skin, utilizing both w/o and o/w emulsions. This transition from emulsion to emulgel occurs with the incorporation of a gelling agent into the water phase [6, 7]. Emulgels offer several advantages in dermatological applications. They are greaseless, easily spreadable, easily detachable, and they behave thixotropically besides that, they are translucent, biodegradable and soluble in water, non-staining, offer an extended shelf- life, and they have emollient qualities [8-10].

Advantages of Emulgel

- APIs that are hydrophobic can be rapidly integrated into the gel foundation utilizing water/oil/water emulsions.
- Improved load capacity as well as stability.
- Simple to produce and a cheap mechanism.
- Avoid sonication.
- The first metabolism is bypassed.
- Prevent stomach-related compatibility.
- Targeted drug administration to the body.
- Increased patient adherence.
- Improved appropriateness and patient acceptance for self-medication.
- The capacity to quickly stop taking medication [11].

Disadvantages of Emulgel

- People with contact dermatitis may have skin irritation as a result of the medication and/or excipients.
- Some drugs have a low skin permeability..
- The possibility of eliciting allergic reactions.
- Medications with larger particle sizes pose challenges in skin absorption [12].

Forms of Emulgel:

1) Macroemulsion Gel

These are the most common types of emulgels that are used when the emulsion droplets are larger than 400 nm. Even though they are clearly opaque, individual drops are plainly distinguishable under a microscope. Thermodynamically, microemulsions are unstable.

2) Nano Emulsion Gel

A nanoemulgel is created when a nanoemulsion is combined with a gel. Transparent or translucent, thermodynamically stable dispersions of water and oil, known as nanoemulsions, are stabilised through a combination of surfactant and co-surfactant surface coating, and the size of droplets are usually smaller than 100 nm. Both *in vitro* and *in vivo*, nanoemulsion formulations show improved transdermal and dermal distribution capabilities. Comparing this development to conventional topical formulations like emulsions and gels has increased the transdermal penetration of many medications.

3) MicroemulsionGel

Microemulsions maintain transparency and thermodynamic stability due to their droplet sizes ranging from 10 to 100 nm, which prevent coalescence. These formulations consist of specific ratios of water, co-surfactant, and oil. Components of microemulsions may increase drug penetration rates by lowering the stratum corneum's diffusion barrier. However, to address this issue, gelling agents like carrageenan, xanthan gum, and carbopol 940 were added to create a gel that is microemulsion based.thereby increasing viscosity for topical application. Despite this enhancement, the low viscosity of microemulsions limits their skin retention capacity. However, microemulsion-based gel formulations encourage greater drug accumulation in the skin for effective action by preventing drug absorption into the bloodstream [13, 14].

Drug Delivery across the Skin

The thickness of the stratified, keratinized squamous epithelium comprising the epidermis, the outermost layer of the skin, varies depending on its location on the body. The thickest area contains elastic filaments, while the relatively waterproof covering formed by the skin protects deeper and more delicate structures underneath. Beneath the skin lies a network of plenty of blood vessels, including an especially large uninterrupted venous plexus that gets blood from dermal capillaries. Additionally, blood has been made available to this plexus directly from tiny arteries in the body's most exposed regions—such as the hands, feet, and ears—through highly muscular arteriovenous anastomoses. Dermatological pharmacology is unique in that it uses the skin as a target organ that is directly accessible for both diagnostic and therapeutic reasons. Serving as a two-way barrier, the skin plays a crucial role in preventing the absorption and loss of electrolytes and water. Topical medication absorption primarily occurs through three pathways: transcellular, intercellular, and follicular routes. Most drugs find their way through the difficult route that circumnavigates corneocytes as well traverses

the lipid bilayer upon the layers of skin's that is healthy. However a pilosebaceous route, although less recognized in clinical settings, is the second most common method of distribution. Similar rates of chemical penetration in isolated stratum corneum and whole skin samples indicate that the barrier to absorption is predominantly found in epidermis or stratum corneum. For multiple decades, topical applications employing painkillers and antibiotics have been administered to affected areas of the body using creams and gels. These include topical creams for skin infections, arthritis pain relief creams, and gels and creams for vaginal yeast infections. Furthermore, other medications can now be absorbed transdermally, allowing for systemic treatment of both the entire body and specific problem areas, such as the skin [15, 16].

Various Ingredients of Emulgel Formulation:

Aqueous Material

The emulsion's aqueous phase is thus created. Usually, water is utillised.

Oils

These elements are essential to for emulsions' oily phase. The physicochemical properties of the oil stage, such as its molecular volume, polarity, and viscosity, play a crucial role in the formulation of emulsions, microemulsions, and nanoemulsions. These properties also have a significant impact on the size of the resulting droplets, the solubility of drugs, and the spontaneity of the emulsification process. In order to facilitate optimal medicine loading, the oil having the highest solubilizing capacity to chosen drug applicant is frequently the ideal oily phase to produce a emulsion, micro-emulsion, and nano-emulsion. Therefore, choosing an oily phase usually entails finding a compromise between the phase's capacity to dissolve the medication and its role in creating an emulsion with the necessary characteristics. Various oil phases, including balsam, birch, castor, myrrh, rose hip, isopropyl myristate, and wheat germ oils, are utilized in the production of emulgels [17–19].

Emulsifiers

Using Emulsifiers allows us to regulate both stability and process of emulsification. Emulsions are inherently unstable due to thermodynamics; however, they can be stabilized by adding the appropriate emulsifying agents. Oil-in-water emulsions are frequently made using surfactants with Hydrophilic-Lipophilic Balance (HLB) values greater than 8, comprised of non-ionic surfactants as spans and tweens. On the other hand, the preparation of water-in-oil emulsions frequently calls for the use of mineral oils with HLB values less than 8, such as liquid paraffin. When compared to either, span or tween systems alone, combinations of span 20 and tween 20 typically produce better emulsion stability [20-26].

Penetration Enhancers

Penetration-enhancing chemicals are frequently used in pharmaceutical vehicles with the goal of temporarily breaking down the skin barrier, fluidizing lipid channels between corneocytes, changing how drugs are partitioned within skin structures, or improving skin transport through other means. These penetration enhancers exhibit specific characteristics.

- ✓ They should not be annoying, poisonous, or allergic.
- ✓ Ideally, they should demonstrate rapid onset, predictable and consistent activity, and a sustained duration of effect.
- ✓ They should refrain from binding to receptor sites or eliciting any pharmacological effects within the body.
- ✓ In order to promote the entry of therapeutic medications into the body and stop the body from losing endogenous material, penetration enhancers must function unidirectionally.
- ✓ It should be possible to incorporate penetration enhancers into a variety of topical therapies while maintaining their compatibility with excipients and pharmaceuticals. They should also preserve appropriate aesthetic qualities and provide a "feel" that is appropriate for skin [27].

Gelling Agents

Emulgels are created by the interaction of gelling compounds in gel bases with emulsions. These chemicals, which are sometimes referred to as thickening agents, expand in the aqueous phase and create gel-like structures, improving the consistency of different dosage forms. When a gelling agent is added, a solution becomes thixotropic. In a comparative study, HPMC-based emulgels exhibited a superior drug release rate compared to Carbopol-based emulgels. Emulgels formulated with NaCMC are particularly suitable for vaginal application, showcasing superior *in vitro* and *in vivo* performance and enhanced mucoadhesiveness, thereby prolonging

medication residence time. On the other hand, HEC-based emulgels demonstrated lower mucoadhesion but displayed favorable drug release profiles and rheological properties. Emulgels containing pemulen as the base are intended for for administering by buccal route [28, 29].

Table 1: Various Gelling Agents Used in Pharmaceuticals Dosage Types

Sr.No.	Gelling Agents	Concentration Used (%w/w)	Pharmaceutical Adaptability	API	Reference
1	Sodium Carboxymethyl Cellulose	3-4%	Stand autoclaving makes it appropriate for sterile gels.	Benzydamine	[30]
2	Carbopol-934	1%	Offer a regulated release for the integrated API.	Chlorphenesin	[31]
3	Carbopol-940	1%	Due to the high viscosity of gel, the API is integrated with controlled release.	Mefenamic acid	[32]
4	HPMC	2.5%	Possessing strong stability, resistance to microbes.	Clorphenesin	[33]
5	HPMC & Carbopol Combination	1.2%	mixture increases stability	Ketorolac, clotrimazole	[34]
6	Pluronic® F127	1-3%	increased solubility in colder water	Piroxicam	[35]
7	Pemulen	0.1-0.4%	Fast oil phase release and superior stability	Flurbiprofen	[36]

Preparation of Emulgel [37-39]

Step 1: Formulation of O/W or W/O Emulsions:

The first stage in creating an emulsion is to dissolve water-soluble compounds in the aqueous phase (tween 80 in filtered water) and oil-soluble substances in the oil phase (Span 20 in liquid paraffin). To guarantee that the two phases are distributed into droplets, they are then mixed together in a turbulent mixing environment. Mechanical stirrers are commonly used in laboratory settings for emulsion preparation, and in industrial manufacture, ultrasonicators, homogenizers, colloid mills, and mechanical stirrers are frequently used for emulsification.

Step 2: Formulation of Gel Base:

Water-soluble substances, also known as excipients, are first solubiliz ed in the aqueous medium by mechanical stirring in a mixing vessel.To prevent aggregation, a hydrophilic polymer is gradually added to a stirred mixture. Until the polymer completely dissolves within the desired pH range, stirring is maintained. Excessive stirring of pharmaceutical gels can lead to air entrapment, necessitating a moderate mixing rate.

Step 3: Addition of Emulsion into Gel Base via Consistient Blending:

The emulsion and gel phases are combined in a 1:1 ratio to generate emulgel.

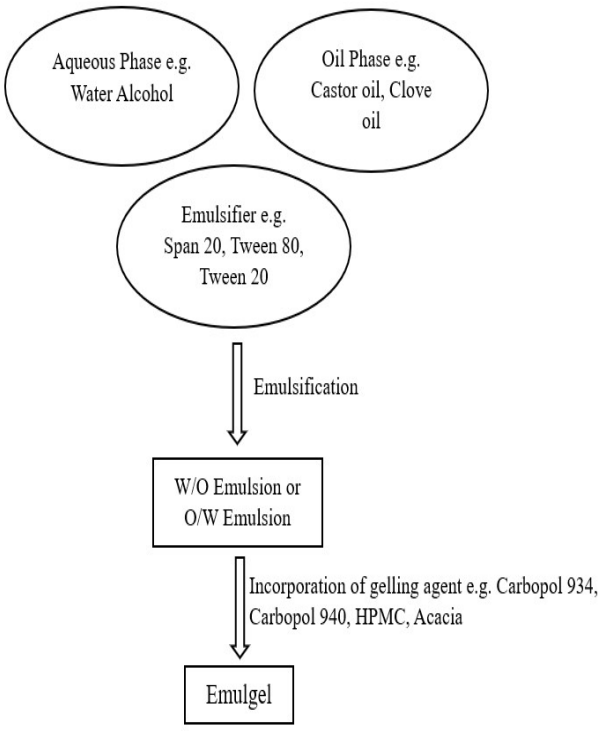

Figure 1: Steps generally taken in emulgel preparation

Characterization of Emulgel:

Physical Examination

The visual evaluation of the resultant emulgel compositions comprised assessing their colour, homogeneity, consistency, and probable phase separation [40].

pH Measurement

To measure the pH of each manufactured emulgel, a digital pH metre is employed. Before employing a standard buffer solution, the pH metre must be calibrated. A consistent suspension is created after dissolving 1 g of the formulation in distilled water, and it is then set aside for 2 hours. The pH level is determined by putting an electrode made of glass into the suspension after two hours [41-42].

Spreadability

In the laboratory study, the apparatus recommended by Mutimer et al. (1956) is suitably modified and employed to measure spreadability. This device is made up of a wooden block with the pulley on one side. Spreadability has been measured using emulgels' "Slip" and "Drag" qualities.This block has a ground glass slide firmly affixed to it, onto which an extra 2 g of emulgel is put for inspection.

The emulgel is then positioned and fastened with a hook between the ground glass slide and a second glass slide with the same measurements. In order to get rid of air bubbles and guarantee a consistent emulgel layer between the slides, a 1 kg weight is put above for five minutes. The borders are meticulously cleaned of any extra emulgel. An 80 gramme pull is then applied to the top plate. A thread attached to the hook is used to measure the amount of time (in seconds) required for the top slide to travel 7.5 cm. A shorter time indicates improved spreadability[43].

Globule Size and Its Distribution in Emulgel

The Malvern Zeta sizer was used to assess the globules' size and dispersion.One gram sample was mixed into a homogeneous dispersion by dissolving it in water that was filtered and stirring. Subsequently, a portion of the sample was introduced into the zetasizer photocell. This procedure yielded the mean globule diameter and dispersion [44].

Drug Content Determination

After dissolving one gramme of the gel formulation in the appropriate solvent, the mixture was filtered to produce a transparent solution. To test the absorbance of the resultant solution, a UV-visible spectrophotometer was employed. The drug calibration curve was utilised to ascertain the drug content [45].

Zeta Potential

The Zetasizer (specifically, the Malvern Zetasizer) is employed to measure the zeta potential of emulgel preparations. This is achieved by placing the formulation in a transparent, single-use zeta cell. Prior to experimentation, samples are placed in cuvettes that have been cleaned with methanol [46-48].

In Vitro Release Study

The drug release investigations were conducted using a Franz diffusion cell with an effective area for diffusion of 3.14 cm^2 and a capacity of 15.5 mL. 200 mg of a gelatinized emulsion were evenly placed to the egg membrane's surface. The egg membrane was clamped within the donor and recipient chambers of the diffusion cell. To dissolve a drug, a recently made PBS solution (pH 5.5) was added to the receptor chamber. We agitated the receptor's compartment using a magnetic stirrer. Samples were taken in 1.0 mL aliquots at prearranged intervals. A UV-visible spectrophotometer was employed to ascertain the amount of drugs inthe samples after the proper dilutions. The entire quantity of medication discharged every time point, was determined using cumulative adjustments were applied. Over time, the total amount of medication released through the egg membrane was evaluated [49-52].

Application of Emulgel in Drug Delivery System

Emulsions Make It Simple for Incorporating Hydrophobic Medicines Into Gels.

Throughout the time gel bases refuse to permit for the solubility of hydrophobic medicines. Oily globules in an aqueous phase produce an o/w emulsion, and emulgels allow hydrophobic medicines to be combined into an oil phase. It is also possible to put this emulsion into a gel base. This shows enhanced drug stability and release over just blending medications into a gel foundation.

Production Feasibility and Low Preparation Cost

Due to the quick and easy emulgel preparation, production feasibility can be boosted. The creation of emulgels does not require any specialized equipment. Additionally, the

materials are inexpensive and easily accessible. As a result, emulgels' production costs can be decreased.

Controlled Release
Emulgels have the potential to extend the duration of action for drugs with shorter half-lives.

Patient Compliance
They are simple to use and less oily.

No Intensive Sonication
While sonication is not necessary for emulgel, it can lead to drug leakage and degradation in vesicular molecules.

Better Loading Capacity
Due to its extensive network, it outperforms alternative techniques like nanosized liposomes and niosomes in terms of loading capacity.

Better Stability
Other preparations, such as hygroscopic powders, creams that phase invert or break, and ointments that get rancid because of their oily bases, exhibit superior stability than emulgels [53].

CONCLUSION

Based on the comprehensive review of emulgels, it's evident that these formulations hold significant promise in various applications due to their unique combination of properties from both gels and emulsions. The review covered a range of aspects including types, ingredients, preparation methods, and characterization approaches, providing a thorough understanding of the subject. Key findings suggest that the type of emulgel, whether oil-in-water or water-in-oil, significantly influences its properties and applications. Moreover, the selection and combination of ingredients play a crucial role in determining the stability, rheological properties, and efficacy of emulgels.

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