



RESEARCH ARTICLE

Emulgel Considered as Anovel Type of Dosage Form for Topical Application

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Emulgels are a topical medication delivery device that has a dual release control mechanism combining gel and emulsion. This formulation aims to transfer hydrophobic medicines into the bloodstream through the skin. When gel and emulsion are used together, the resulting dosage form is called Emulgel. Hydrophobic medications are often formulated in an oily basis and administered to the skin using emulgel. Emulgels have advantages in terms of adhesion, spreadability, viscosity, and extrusion. Additionally, they will serve as an optimal method for incorporating hydrophobic medicines into water-soluble gel bases. Emulgels possess several advantageous characteristics for dermatological applications, including thixotropy, non-staining, non-greasy, easy spreadability, extended shelf life, emollient qualities, easy removal, transparency, and aesthetically pleasant appearance. This study focuses on the utilization of emulgel-based systems as drug delivery vehicles, highlighting current advancements and future prospects.

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INTRODUCTION

Although topical drug delivery has a long history, new technologies and methods are continuously being researched. The skin, being the most accessible organ, has the potential to enhance drug delivery efficacy compared to other routes of administration. Recent technological advancements have further improved this field.

It is capable of delivering drugs to the skin and throughout the body. This method is one of the better choices for cutaneous applications.⁽¹⁾ Topical drug delivery refers to the administration of a medication. Topical medication used to treat skin disorders directly. Topical medication administration involves the use of topical agents such as ointments, creams, and lotions, which sometimes have a sticky consistency that can make patients uncomfortable during application. Additionally, they have a lower spreading coefficient and need application by rubbing. ⁽²⁾ They also demonstrate issues with stability. To address these issues, the utilization of transparent gels has risen significantly. in cosmetics and medical preparations A gel is a colloid composed of 99% liquid by weight, confined by surface tension between the liquid and a macromolecular network of gelatin fibers. Gels are formed by a process of chemical or physical cross-linking. Entrapment of significant quantities of water or hydroalcoholic liquid inside a network of colloidal solid particles. Gel

formulations typically offer quicker medication release than ointments and creams. Despite the numerous benefits of gels, major One restriction is their incapacity to transport hydrophobic medications. An emulsion-based strategy is being utilized to circumvent this constraint, enabling the effective incorporation and delivery of a hydrophobic medicinal moiety through gels. Emulgels are created by combining gels and emulsions in dosage forms. Emulsions exhibit a certain level of sophistication and may be readily removed from the skin. They possess a high level of skin penetration capacity. Emulgels for dermatological application include advantageous characteristics like thixotropy, non-greasy texture, effortless spreadability, easy removal, emollient qualities, non-staining formula, water solubility, extended shelf life, environmentally friendly composition, and transparency & attractive look. (3) Emulsions are systems designed for controlled release, consisting of two phases that do not mix, where one phase is disseminated throughout the other phase using an emulsifying agent to maintain stability. Emulsions can be of oil-in-water or water-in-oil form, with the drug particles confined in the internal phase moving through the exterior phase. gradually penetrates the skin to deliver a regulated impact. Gel, according to USP, is a semisolid system composed of dispersions of tiny inorganic particles or big organic molecules surrounded and pierced by liquid. (4) The gel includes a higher concentration of An aqueous or hydroalcoholic liquid contained within a cross-linked network of colloidal solid particles that traps tiny drug particles and controls the release of the drug. The liquid phase accumulates. Three-dimensional polymeric matrix formed by physical or chemical cross-linking. The text is minimal Continuous structure leads to solid-like behavior that is homogeneous and obvious. Both the emulsion and gel have a role in regulating the drug release from the systems. (4,5)

Benefits of using emulgel over conventional topical dosage forms

- Emulgel has superior stability compared to other transdermal preparations. For instance, powders are prone to absorbing moisture, creams exhibit phase inversion upon breaking, and ointments can become rancid due to their oily phase (6).
- Emulgels have a higher loading capacity because of their extensive network, whereas niosomes and liposomes are nanosized and feature vesicular structures. Niosomes and liposomes are associated with leakage and lower trapping effectiveness.
- Hydrophobic medications have solubility barriers preventing direct incorporation into gel, leading to issues during drug release. Emulgel facilitates the integration of hydrophobic medicines into oil. phase and then oily globules are dispersed in aqueous phase resulting in o/w emulsion. This o/w emulsion can be mixed into a gel base (7) .
- The emulgel preparation process consists of concise and straightforward procedures, enhancing the production's practicality.
- No specialist tools are required to prepare emulgel. Furthermore, the materials utilized are readily accessible and cost-effective. This lowers the total production expenses of emulgels.
- Production of vesicular preparations like niosomes and liposomes requires intense sonication. Emulgels can extend the duration of action of medications having a short half-life.
- They are less oily and simple to apply (8).

Disadvantages of Emulgel

- Limited medication absorption via the skin
- Skin irritation causing contact dermatitis
- Potential for allergic responses
- Drugs with a high particle size are difficult to be absorbed transdermally.
- The formation of bubbles during the emulgel formulation process (9,10).

Composition of Emulgel preparation

The components of Emulgel formulation consist of five primary elements.: (8,9,10)

- **Aqueous material**

This forms the aqueous phase of the emulsion. Commonly water and alcohol are used for this purpose.

- **Oils**

These components make up the oily component of the emulsion. Mineral oils, with or without soft or hard paraffin, are commonly employed as the carrier for drugs and as an occlusive substance in topically applied emulsions.

- **Emulsifiers**

Emulsifiers are utilized to facilitate emulsification and maintain stability over the product's shelf life. Polyethylene glycol stearate, Sorbitan monooleate (Span 80), Polyoxyethylene sorbitan monooleate (Tween 80), Stearic acid, and Sodium stearate are suitable for this use.

- **Gelling agent**

These compounds enhance the uniformity of any dose form and function as thickening agents. Carbopol 934, Carbopol 940, and HPMC 2910 are gel-forming chemicals utilized in emulgels. These components make up the oily component of the emulsion. Regarding Externally applied emulsions, mineral oils containing soft or hard paraffin, are commonly employed as a carrier for the medicine and as an occlusive substance. Gelling agents utilized in the formulation of Emulgel (Carbopol-934, Carbopol-940, HPMC-2910)

- **Permeation/Penetration enhancers**

These chemicals penetrate and interact with skin components to cause a transient and reversible increase in skin. Clove oil and menthol can serve as permeation enhancers. Penetration enhancers can function through one or more of three primary mechanisms:

1. Disruption of the organized arrangement of stratum corneum lipid. teraction with intercellular protein.
2. Enhanced penetration of the medication, co-enhancer, or solvent into the stratum .

An example of the application of penetration enhancers in emugel dose form is (Clove oil, Menthol,AND Cinnamon). temporary and reversible enhancement in skin permeability. They temporarily disturb the skin barrier, make the lipid channels between corneocytes more fluid, change how the medication is distributed in skin structures, or improve the drug's transport into the skin.

Ideal Properties of Drug to Formulate As Emulgel

- Administer a low drug dosage, namely below 10mg..
- The drug's molecular weight should not exceed 400 Daltons.
- Drug has a half-life of 10 hours or less.
- Log P (octanol-water) partition coefficient ranges from 0.4 to 0.8.
- Skin permeability coefficient should exceed 0.5×10^{-3} cm/hr. • Oral bioavailability and therapeutic index must be low.
- The drug should be non-irritating, non-sensitizing, and have low polarity (11).

Emulgel preparation

The emulgel preparation involves three processes ^(12,13):

Step 1: Create an emulsion, choosing between oil-in-water (O/W) or water-in-oil (W/O) formulations.

Step 2: Creating the gel base

Step 3: Integrate the emulsion into the gel base while swirling continuously. The gel is created by dispersing Carbopol 934 and Carbopol 940 in filtered water with continuous stirring at a moderate pace. The pH is regulated to a range of 6-6.5 by use triethanolamine (TEA).

The oil phase of the emulsion is created by dissolving Span 20 in light liquid paraffin, and the aqueous phase is made by dissolving Tween 20 in filtered water. Methyl and propyl paraben are dissolved in propylene glycol, whereas the medicine is dissolved in ethanol, then combining both solutions in the water phase. Both the oily and aqueous phases are individually heated to temperatures between 700 and 800 degrees Celsius. Subsequently, the oily phase is The substance was introduced into the liquid phase while being stirred constantly and then allowed to cool to room temperature. Glutaraldehyde is incorporated into the emulsion-gel mixture in a 1:1 ratio to create the emulgel.

Emugel release

Choosing the right emulgel excipients is crucial for ensuring the optimal release of active substances, their penetration through biological barriers (such as skin or intestinal mucosa), and ultimately their biological or pharmacological effects. Controlled release and targeted drug delivery may be accomplished by using dual controlled release mechanisms including an emulsion and a gel system ⁽¹⁴⁾. In addition to the physiochemical properties of the active substances and physiological factors, formulation factors significantly influence the release and membrane transport of active substances. The size of particles in a colloidal system, such as an emulsion or an emulgel, significantly influences the release of compounds contained inside the particles. Smaller particle sizes enhance the release and skin penetration of active substances. Surfactants impact medication release by influencing the size of oil droplets and the structure of lipid particles while dispersing and emulsifying one phase in another. Polymers used as gelling agents in emulgels improve the physical stability of an emulsion by boosting the viscosity of the continuous phase, resulting in a delayed release of active ingredients. An increase in drug loading in a formulation speeds up release rates, especially when penetration enhancers are included in emulgels⁽¹⁵⁾.

EVALUATION OF EMULGEL PHYSICAL APPEARANCE

The produced compositions were visually examined for color, homogeneity, and consistency.

- **pH:** ⁽¹⁵⁾ A gram of gel was dissolved in 100ml of pure water, let to stand for two hours, and then the pH was measured using a digital pH meter. pH levels should fall between the range of 5 to 6, comparable to the skin's pH of 5.5, to prevent the danger of irritation.
- **Spreadability:** ^(15,16) The spreading coefficient was determined based on the 'Slip' and 'Drag' properties of emulgels. A gram of emulgel was sandwiched between two glass slides and subjected to a 500 g load for 5 minutes to remove air and create a consistent emulgel layer between the slides. The second glass slide comes with a hook. Weight measurement the object was suspended in the pan using a hook connected to the pulley. The time was measured. Required to slip off the slides lesser the time taken for separation of two slides, better the spreadability. Spreadability was calculated using formula $S = M \cdot L / T$ Where M = wt. tied to upper slide L = length of glass slides T = time taken to separate the slides. Extrudability^[35] The object was

suspended in the pan using a hook connected to the pulley. Time was quantified. Obligated to remove the slides. The quicker the separation of two slides, the better the spreadability. Spreadability was calculated. The test was repeated and the mean data were utilized for the computation. Extrudability calculation formula Extrudability is the amount of force needed to push emulgel out of a tube. $(\text{gm})/\text{Area} (\text{cm}^2)$

- **Viscosity:**⁽¹⁷⁾ Viscosity Measured using a Brookfield viscometer RVT utilizing a cone and plate configuration with spindle No.7. The highest shear rate was 100 revolutions per minute (RPM) while the lowest shear rate was 10 RPM.
- **Swelling Index:**⁽¹⁸⁾ A formulation with a high swelling index has a strong ability to absorb exudates from a wound. The swelling index is determined by depositing 1 gram of emulgel on porous aluminum foil, which is then placed in a petri dish containing 10 ml of 0.1 Sodium Hydroxide. Samples were subsequently extracted from the dish at various time intervals and then placed in a dry location for a period of time before reweighing it. The swelling index was determined using a specific algorithm. Swelling Index (SW) % = $[(W_t - W_o)/W_o] \times 100$ Where (SW) % = Equilibrium percent swelling, W_t = Weight of swollen emulgel after time t , W_o = Original weight of emulgel at zero time.
- **Photomicroscopy:**⁽¹⁹⁾ Emulgel was examined using a light microscope to analyze the globular structure within the gel foundation. The emulgel was appropriately thinned, placed on a glass slide, and seen under a light microscope at a magnification of 40x.
- **Dilution test:**⁽²⁰⁾ 50 to 100 The emulgel was diluted many times by adding the continuous phase and then visually inspected for phase separation and clarity.
- **Drug content:**⁽²¹⁾ One gram of emulgel is combined with an appropriate solvent, subjected to sonication, and then filtered using Whatman filter paper no. 41 to get a transparent solution. The absorbance of the solution is measured using a UV spectrophotometer after it has been appropriately diluted. A standard drug solution is made using the same solvent. Focus Drug content may be determined by using a standard plot and inserting the absorbance value into the standard equation. Drug Content = $(\text{Concentration} \times \text{Dilution Factor} \times \text{Volume taken}) \times \text{Conversion Factor}$.
- **Rheological study:**⁽²²⁾ In Study of the flow properties of materials The viscosity is measured at 25 °C. The equipment utilized is a cone and plate viscometer.
- **In vitro drug release study:**⁽²³⁾ The process is conducted using a Franz diffusion cell. It aids in determining the drug's release.
- **Microbiological assay:**⁽²⁴⁾ The Ditch plate approach is utilized for this strategy. This approach is used to assess the bacteriostatic or fungistatic action. Accelerated stability testing: It is conducted according to ICH recommendations. The stability test is conducted in a hot air oven 37 ± 2 °C, 45 ± 2 °C and 60 ± 2 °C for 3 months .
- **Globule size and distribution in emulgel:** It is determined using the Malvern Zetasizer. The emulgel is dissolved in water, stirred, and then placed into the device for value determination.
- **Centrifugation study:**⁽²⁴⁾ This approach is utilized to assess the stability of an emulgel. It is completed following one week of preparation. The investigation was conducted using a minicentrifuge at 3000 revolutions per minute for 30 minutes.
- **Skin irritation test:**⁽²³⁾ This test is very important because The preparation is a topical formulation. The test is conducted on the animal hide. The emulgel is administered to the animals' skin before they are placed back into their cages. The animals are evaluated after 24 hours. The emulgel is then removed from the location and cleaned with tap water.

EMULGEL CLASSIFICATION

Emulgel may exist in many forms based on the size and distribution of droplets: macroemulsion gel, nanoemulgel, and microemulsion gel. ⁽²⁴⁾

1. Macroemulsion Gel

Macroemulsion gels are the predominant form of emulgels. Droplets in emulgel typically have a particle size larger than 400 nm, causing the emulgel to appear opaque and allowing individual droplets to be plainly visible under an optical microscope. Macroemulsions, similar to other emulsions, are thermodynamically unstable systems that may be stabilized by surface-active chemicals. ⁽²⁵⁾

2. Nanoemulgel

Nanoemulgels are formed when a nanoemulsion is added to a gel. Nanoemulsion is a very effective delivery strategy for lipophilic and poorly bioavailable medicines when compared to other nanolipid delivery technologies. Nanoemulsions are isotropic systems that are optically transparent or translucent. Nanoemulsions provide advantages such improved physical stability, increased drug-loading capacity for both lipophilic and hydrophilic medicines, and greater solubility. Nanoemulsion formulations have superior transdermal and dermal distribution characteristics in both laboratory settings and living organisms as compared to traditional topical formulations. Nanoemulsions typically have a particle size ranging from 100 to 400 nm. Nanoemulsions, with their tiny particle size, possess a larger surface area that allows for enhanced absorption. The small size of nanoparticles enhances the effectiveness of medications in penetrating biological barriers, such the skin. Algahtani et al. developed a nanoemulgel containing thymoquinone that exhibited enhanced skin penetration and deposition properties upon topical application compared to a traditional hydrogel. ^(26,27)

3. Microemulsion

Microemulsions are thermodynamically stable systems that are transparent, isotropic, and consist of water, oil, surfactant, and a cosurfactant. The droplet size typically falls within the range of 10–100 nm. Microemulsions exhibit characteristics including transparency, low viscosity, and tiny particle size. They may develop spontaneously, unlike traditional emulsions. Furthermore, microemulsions exhibit no phase separation throughout a broad temperature range⁽²⁸⁾. Microemulsions exhibit distinct differences compared to nano- and macroemulsions. The first distinction is in the size of the particles, followed by the formation and stability. Nanoemulsions need a reduced amount of emulsifier for their manufacture in comparison to microemulsions. Microemulsions are very stable and can maintain their stability for several years⁽²⁹⁾. The droplet size is not the only factor that influences the thermodynamic stability of a system. Microemulsions often include high levels of emulsifiers, exceeding 10%, and are frequently combined with cosurfactants such amphiphilic short-chain alcohols or their esters to provide structural support. The molecular composition and concentrations of surfactants and cosurfactants dictate the microstructure of the system. When selected correctly, they provide a tightly integrated layer at the oil-water contact. Microemulsions develop spontaneously and are defined by the presence of tiny, uniformly-sized droplets⁽³⁰⁾. Microemulsion's drawback is its restricted application caused by its low viscosity, resulting in less product contact with the skin. Viscosity-increasing agents are added to the microemulsion system to create a gel microemulsion, which helps in achieving the desired viscosity and extending the release of the active component.

PACKAGING OF EMULGELS ^(32,33,34,35)

Emulgels are typically packaged in lacquered aluminum tubes with a membrane seal and an interior coating of phenoxy-epoxy based lacquer. The tubes are capped with a propylene screw cap⁽³¹⁾. Aluminum tubes sealed with a molded seal and a polypropylene screw cap. laminate tubes Oil laminates material It offers a barrier to light, air, and moisture, and includes all plastic laminates. It features a chemical-resistant barrier.

The preparations of emulgel that are market commercially are listed below in table 1

Product Name	Drug	Manufacturer	USES
Voltaren™	Diclofenac Diethyl Ammonium	Novartis Pharma	Antiinflammatory
Miconaz-H-emulgel™	Miconazole Nitrate, Hydrocortisone	Medical Uniun Pharmaceutical	Topical corticosteroid & antifungal
Diclomax Emulgel™	Diclofenac Diethyl Amine	Torrent Pharma	Antiinflammatory
Dermafeet Emulgel	Urea 40%	Herbitas	Intense moisturizing and exfoliation activity
Denacine emulgel	Clindamycin phosphate	Beit jala pharmaceutical company	Antiacne
Isofen emulgel	Ibuprofen	Beit jala pharmaceutical company	Antiinflammatory
Diclona emulgel	Diclofenac diethylamine	Kuwait Saudi pharmaceutical industries co.	Antiinflammatory
Cataflam emulgel	Diclofenac potassium	Novartis	Antiinflammatory
Miconaz-H-emulgel	Miconazole nitrate, Hydrocortisone	Medical union Pharmaceuticals	Topical corticosteroid and antifungal

SUMMARY

Topical medication delivery systems utilize several formulations, each with its own drawbacks. Emulgel preparation overcomes most of these drawbacks. The emulgel has been demonstrated as the most convenient, superior, and effective delivery technology in the project. Combining emulsion with gel creates a dual control release mechanism, addressing issues including phase separation, creaming, and enhancing stability. Emulgel requires components similar to those found in emulsions

and gel preparations. The emulgel is prepared by three steps: emulsion preparation, gel preparation, and integration of the two preparations. Each formulation requires a thorough assessment. Here, there are around twenty-five assessment methods, including light microscopy, spreadability, rheological study, and in-vitro drug release study. Currently, emulgel is extensively utilized. Commonly used emulgels include Miconaz-H emulgel, Isofen emulgel, and Diclon emulgel. Emulgels are typically utilized as anti-inflammatory medications.

CONCLUSION

Most novel therapeutic compounds are hydrophobic, posing a challenge for researchers to administer them in any dosage form due to their low solubility. Formulating hydrophobic medicines for topical delivery has always been a tough challenge. When administering these medications in traditional forms as cream, ointment, lotions, or emulsion, stability and bioavailability issues arise because of their hydrophobic properties. Hydrophobic medications are difficult to distribute effectively using gel formulations due to the very negligible results obtained. The novel notion of emulsion formulation Gel has demonstrated improved drug delivery by including the drug in the oil phase of an emulsion, which is then stabilized in the gel. This combination of phases provides a controlled release effect, enhancing the bioavailability of the medications. The benefits of emulgel provide significant potential for delivering hydrophobic drugs topically with increased effectiveness and reduced production costs in the future. Therapeutic oils Enhance the synergistic action of the emulgel.

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