

## Review on: - Emulgel: A Emerging Trend in Topical Drug Delivery System

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### ABSTRACT-

Gels appear to be more advantageous in both cosmetics and pharmaceutical preparations when compared to other semisolid formulations. When gel and emulsion are combined, the result is emulgel. Emulgel is a promising drug delivery system that can be used to administer hydrophobic medications.

Emulgel, a fascinating topical drug delivery system, employs a dual release control system comprised of gel and emulsion. Emulgel has a number of advantages, including the fact that it is greaseless, easily spreadable, removable, emollient, and transparent.

To make emulgel, the incorporation method is used. Emulgels are frequently used to deliver analgesics, anti-inflammatory medications, anti-fungal medications, anti-acne medications, and various cosmetic formulations. Because of its superiority over other methods, studies on emulgel promise a brighter future in terms of delivering more topical drugs as emulgel.

**KEYWORDS:** -Emulgel, Topical Drug Delivery System, Emulsion, Gel

### I. INTRODUCTION-

Illness has been treated in recent decades by administering drugs to the human body. Parental administration can take place via a variety of routes, including oral, sublingual, and rectal. The

administration of topical drugs is a localised process. Drug delivery system capable of delivering medications to any part of the body. Topical routes include ophthalmic, rectal, vaginal, and skin administration.

These employ a diverse range of cosmetic and dermatological preparations to their healthy or skin disease. A variety of conditions are treated with topically applied drugs..

Their action at the application site or for systemic effects. Drug absorption through the skin is enhanced when a drug substance is in solution and has a high solubility. If the lipid/water partition coefficient is greater than zero, the electrolyte is present. Drugs used locally that are applied to the skin. In the action, antiseptics are used.

Gels are a relatively newer type of dosage form that is formed by entrapping large amounts of aqueous or other liquid. A colloidal solid network containing hydro-alcoholic liquid particles composed of inorganic substances such as aluminium salts or natural organic polymers or synthetic polymers with a higher aqueous concentration..

Component that promotes greater drug dissolution and easy drug migration via a vehicle that is essentially a liquid, as opposed to an ointment or cream base [5]. Despite numerous advantages, these are superior in terms of use and patient acceptability. One significant limitation of gels is in the delivery of hydrophobic drugs.

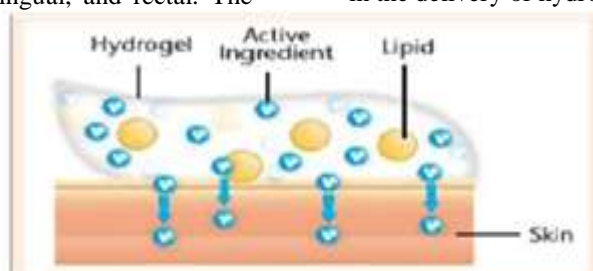


Fig-Emulgel Structure

Sr no	Title name	Author name	Remark
1	Formulation and Evaluation Of ornidazole Topical Emulgel	K. Raju, G. Sneha, Rokayya Khatoon, M. Ashwini, G. Shirisha	Carbapol 934 with liquid paraffin showed superior drug release patterns with Ornidazole in Emulgel
2	Studies on the Development of Promising Herbal Emulgel of Coccinia Grandis Leaf Extract for Dermatological Complications	Gayathri Guntupalli, Gudelli Manisha Rani, Lakshmi Prasanthi Nori, S.S. Manikiran	Topical emulgel of Coccinia grandis leaf extract can be used for the bacterial skin infections.
3	Formulation and Evaluation of Emulgel of Clindamycin Phosphate for Effective Treatment of Acne	Priya Ranjan, Vivek Jain, Shradha Shende, Prabhat Kumar Jain	All the prepared emulgel showed acceptable physical properties. The best formulation F4 showed better antiacne activity compared with all formulation.
4	Formulation and evaluation of oxiconazole Emulgel for Topical Drug Delivery	Venkateswara Rao, S., Vijaya Sri, P. and Padmalatha, K.	Formulation F1 showed better releasing of drug than comparison with oxiconazole marketed cream.
5	Formulation and evaluation of mefenamic acid emulgel for topical delivery	Rachit Khullar *, Deepinder Kumar, Nimrata Seth, Seema Saini	Topical emulgel of mefenamic acid possess an effective anti-inflammatory and analgesic activity

#### RATIONALE-

Many topical agents, such as ointment, cream, and lotion, have numerous disadvantages. They are extremely sticky when applied, causing discomfort in the patient. Many topical agents, such as ointment, cream, and lotion, have numerous disadvantages. They are extremely sticky when applied, causing discomfort in the patient.

They also have a lower spreading coefficient and must be applied rubbing. They also have a problem with consistency. The use of transparent gels in cosmetics and pharmaceutical preparations has increased as a result of all of these factors within the major group of semisolid preparations. A gel is a colloid that is typically 99

percent liquid and is held in place by surface tension between it and a macromolecular network of fibres made up of a small amount of a gelating substance. Despite many advantages, one significant limitation of gels is the delivery of hydrophobic drugs. An emulsion-based approach is being used to overcome this limitation, allowing even a hydrophobic therapeutic moiety to be successfully incorporated and delivered via gels..

There has been a lot of interest in using novel polymers with complex functions as emulsifiers and thickeners in recent years because their gelling capacity allows the formulation of stable emulsions and creams by decreasing surface and interfacial tension while increasing aqueous

phase viscosity. The presence of a gelling agent in the water phase, in fact, converts a conventional emulsion into an emulgel. Both oil-in-water and water-in-oil emulsions are used to deliver drugs to the skin.

Emulgels for dermatological use are thixotropic, greaseless, easily spreadable, easily

removable, emollient, nonstaining, water-soluble, have a longer shelf life, are bio-friendly, transparent, and have a pleasing appearance. Emulgel allows for dual drug release control from the formulation.

Sr. no.	Marketed Products( Brand Name)	Manufacturing Company
1	Volini Gel	Ranbaxy Laboratories
2	DiclonEmulgel	Med Pharma
3	Voltaren	Novartis Pharma
4	Voltarol Emulgel P	Glaxo Smith kline Pharma
5	Isofen Emulgel	Beitjala Pharma

#### Advantages-

Using o/w emulsions, hydrophobic drugs can be easily incorporated into gels. Because solubility acts as a barrier during drug release, most hydrophobic drugs cannot be incorporated directly into gel bases. Emulgel facilitates the incorporation of hydrophobic medications. This may provide better drug stability and release than just using the gel base.

1. Greater stability: Emulgels are more stable than other transdermal preparations. Powders are hygroscopic, creams suffer from phase inversion or breaking, and ointment suffers from rancidity due to an oily base.
2. Increased loading capacity: Other novel approaches, such as niosomes and liposomes, are nanosized and may result in leakage and lower entrapment efficiency due to vesicular structures.
3. Greater patient acceptance
4. Provide individualised drug administration.
5. Simple therapy discontinuation.
6. Increase bioavailability; when compared to other conventional semisolid preparations, even low doses can be effective.
7. Stable formulation achieved by lowering surface interfacial tension and increasing aqueous phase

viscosity; more stable than transdermal preparations; powders are hygroscopic; creams exhibit phase inversion or breaking; and ointment exhibits rancidity due to oily components

6. Increase bioavailability; when compared to other conventional semisolid preparations, even low doses can be effective.
7. Stable formulation achieved by lowering surface interfacial tension and increasing aqueous phase viscosity; more stable than transdermal preparations, which are less stable in comparison; Powders are hygroscopic; creams suffer from phase inversion or breaking; and ointment suffers from rancidity due to oily components..

#### Disadvantages-

1. Inadequate macromolecule absorption
2. Entrapment of bubbles during formulation
3. Hydrophobic drugs are the best choice for such delivery systems.
4. Skin irritation or allergy reaction due to contact dermatitis
5. Only applicable to drugs that require a very low plasma concentration to be effective.
6. Drugs may be denatured by an epidermal enzyme. Patents of Emulgel.

Sr no	Title	Application No.	Year
1	Diclofenac diethylamine emulgel and preparation method thereof	CN102525886A CN10CN102525886A CN2012100099041A2525886A	2013
2	Organo-gel	US20060078577A1	2010

	formulations for therapeutic applications	US20060078577A1	
3	Emulsified gel composition	US20200397694	2019
4	Method for treating a protozoal infection	US10561650B2	2020
5	Besifloxacin for the treatment of resistant acne	EP3099301B1	2019

**Emulgel Formulation -**

Sr no	Ingredients	Used as
1	Carbopol, HPMC	Polymer
2	Light liquid paraffin	Oily vehicle
3	Span 20/80	Surfactant for oil phase emulsion
4	Tween 20/80	Surfactant for Aqueous phase emulsion
5	Propylene Glycol	humectant
6	Methyl/ propyl paraben	preservative
7	Lemon oil, eucalyptus oil,	Penetration enhancer

There are various types of emulsions based on the size of the droplets and the nature of the distribution.

- 1] Macro emulsion gel
- 2] Nano emulsion gel
- 3] Micro emulsion gel

**1) Macroemulsions gel**

With droplet particle sizes greater than 400nm, these are the most common types of emulgels. They are visually opaque, but under a microscope, the individual droplets can be seen. Macroemulsions are thermodynamically unstable, but surface active agents can help to stabilise them. Khullar R. et al, for example, used Carbopol 940 as a gelling agent to create mefenamic acid emulgel. The oil phase consisted of liquid paraffin. Menthol and clove oils were used to improve penetration. It was then evaluated for rheological studies, spreading coefficient studies, skin irritation tests, in-vitro release, and other purposes.

**2) Nanoemulsion gel**

Nanoemulgel is formed when nanoemulsion is combined with gel.

Nanoemulsions are transparent (translucent) thermodynamically stable oil-water dispersions stabilised by an interfacial film of surfactant and cosurfactant molecules with droplet sizes less than 100nm. In vitro and in vivo, nanoemulsion formulations have improved transdermal and dermal delivery properties. Many drugs now have higher transdermal permeability than in traditional topical formulations like emulsions and gels..

**3) Microemulsion gel:**

Microemulsions are transparent and thermodynamically stable because their droplet size ranges from 10 to 100nm and they do not coalesce. Microemulsions are created by combining specific amounts of oil, co-surfactant, and water. Microemulsion ingredients may improve drug permeation by lowering the stratum corneum diffusion barrier. Microemulsions, on the other hand, have a low retention capacity in the skin due to their low viscosity, limiting their application in the pharmaceutical industry. To address this shortcoming, gelling agents such as Carbopol 940, xanthan gum, and carrageenan were mixed into the Microemulsion to create a gel with increased

viscosity that could be used topically. Additionally, the microemulsion-based gel inhibits drug absorption in the body.

### 1. Emulgel formulation

#### a) Vehicle-

The following are the vehicle's specifications:

1. Deliver the medication to the correct location.
2. Maintain a therapeutic drug level in the target tissue for long enough for a pharmacological effect to occur.
3. Allow the medication to migrate freely to the site of action.

#### b) Aqueous liquid

The aqueous phase of the emulsion. Water and alcohol are two common agents.

#### c) Mineral oils

These are agents of the oily phase. Mineral oils are commonly used in externally applied emulsions, either alone or in combination with soft or hard paraffins. As nutritional supplements in oral preparations, non-biodegradable mineral and castor oils with a local laxative effect, as well as fish liver oils or various fixed oils of vegetable origin (e.g., arachis, cottonseed, and maize oils), are used.

### 2) Agent for emulsification

Emulsifying agents are used in the manufacturing process to promote emulsification and to maintain shelf stability. Some examples include Sorbitan mono-oleate (Span 80), Polyoxyethylene Sorbitan monooleate (Tween 80), Stearic acid, and Sodium stearate.

### 3) Thickening agent

These are used to improve the consistency and gelled behaviour of dosage forms. There are two kinds of gelling agents: natural and synthetic. A system becomes thixotropic when a gelling agent is added to it. The concentration of gelling agent is discovered to have an inverse relationship with the amount of drug released. Following that, hydrate and swell. Because of its hydrophilic nature, cross-linked structure, and insolubility in water, carbopol is a potential candidate for use in controlled release drug delivery systems. In terms of drug release, HPMC emulgel outperforms carbopol. For instance, carbopol-934 (1%) and HPMC-2910 (2.5 percent).

Propyl paraben and methyl paraben are two examples of preservatives.

Butylated Hydroxyl Toluene (BHT), Ascorbyl palmitate, Butylated hydroxyanisole (BHA), and other antioxidants

**6) Humectants:** used to keep moisture in the air. Glycerin, propylene glycol, and other similar substances are examples.

**7) Gelling agents:** These are agents that are used to thicken and increase the consistency of any dosage form. Examples include carbapol 934, carbapol 940, HPMC, and sodium CMC.

**8) Permeation enhancers:** are agents that partition into and interact with skin constituents to increase skin permeability temporarily and reversibly. Some examples include oleic acid, lecithin, isopropyl myristate, urea, eucalyptus oil, and menthol.

A penetration enhancer should be non-toxic, non-irritating, and non-allergenic, and its activity and duration of effect should be predictable and reproducible.

- They must not have any pharmacological activity in the body, meaning they cannot bind to receptor sites.

- The penetration enhancers should be unidirectional in order to allow therapeutic agents to enter the body while preventing endogenous material loss.

- The penetration enhancers should be compatible with both excipients and drugs and should be suitable for formulation into a wide range of topical preparations.

#### ➤ Penetration Enhancer Mechanism

Penetration enhancers can function in one of three ways.

1. Disruption of the highly ordered structure of the stratum corneum lipids.
2. Interaction with a protein in the extracellular space.
3. Enhancement of drug, co-enhancer, or solvent partitioning into the stratum corneum.
4. Because solubility acts as a barrier during drug release, most hydrophobic drugs cannot be incorporated directly into gel bases.
5. Emulgel facilitates the incorporation of hydrophobic drugs into the oil phase, after which oily globules are dispersed in the aqueous phase, yielding an o/w emulsion that can be mixed into a gel base. Drug stability and release may be improved over simply incorporating drugs into a gel base.

### PREPARATION METHOD

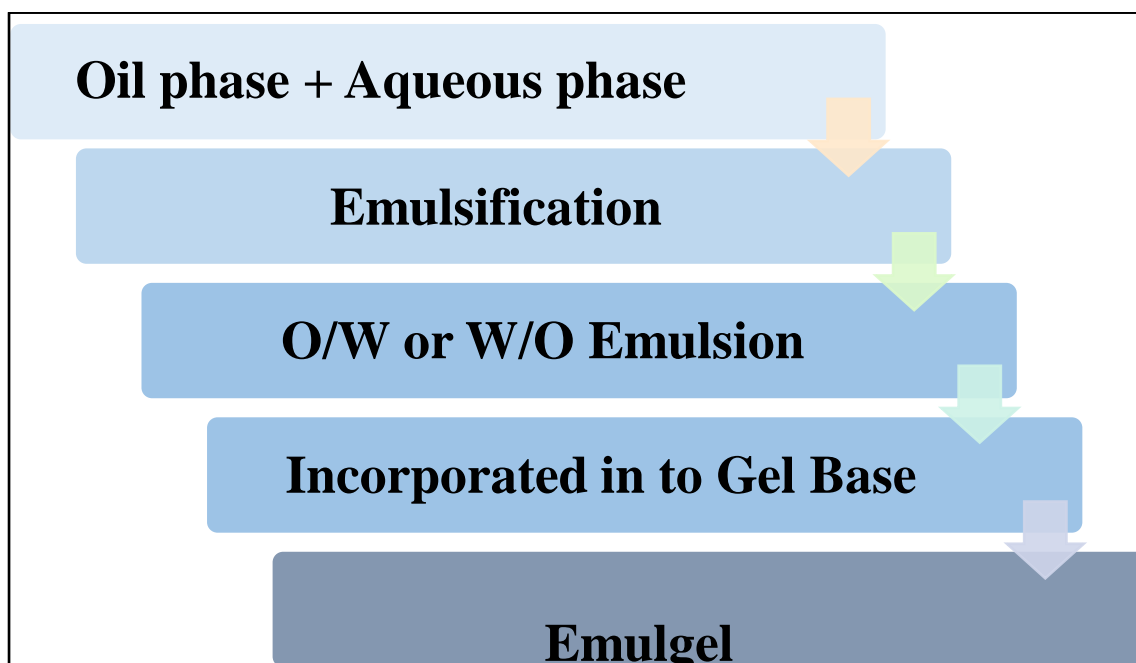
It consists of three steps.

**Step 1:** emulsion formulation, either o/w or w/o oil phase preparation: the oil phase of the emulsion is prepared by dissolving the emulsifier. In the oil phase, for example, span 20 is made up of light liquid paraffin.

**Preparation of the aqueous phase:** The aqueous phase is prepared by dissolving the emulsifier. Tween 20 in purified water, for example.

**Step 2:** gel base formulation: polymer was dispersed in purified water using a mechanical shaker at a moderate speed, and the pH was adjusted to 6-6.5 using tri ethanolamine (TEA).

**Step 3:** Incorporate emulsion into gel base: To make emulgel, mix gel and emulsion in a 1:1 ratio with glutaraldehyde.



### Formulation

#### 1. Making an Emulsion

##### A) Preparation of the Aqueous Phase:

The aqueous phase of the emulsion was created by dissolving tween 80 in purified water.

##### B) Preparation of the Oil Phase:

Methyl paraben and propyl paraben were dissolved in propylene glycol, while the drug was dissolved in ethanol, and the two solutions were mixed with aqueous phase. After heating the oily and aqueous phases separately to 75 degrees Celsius, the oil phase was added to the aqueous phase with continuous stirring until it cooled to room temperature.

**2. Gel preparation:** To make the gel bases, different polymer concentrations were dispersed in distilled water separately while a mechanical shaker was used to constantly stir at a moderate speed. The pH of all formulations was adjusted to 6 - 6 using triethanolamine. 5. Utilization of triethanolamine (TEA).

**3. Emulgel Preparation:** To make the emulgel, the obtained emulsion was gently mixed with the gel.

### Evaluation Parameters of Emulgel-

**1. Physical appearance:** The prepared Emulgel's colour, homogeneity, consistency, and phase separation are all visually checked.

**2. PH Evaluation:** The pH of a formulation is an important criterion to consider, especially for topical formulations. The pH of the emulgel should be between 5.8 and 6 to mimic the skin condition. The patient may experience irritation if the pH of the prepared emulgel is acidic or basic. The prepared emulgel's PH was determined by dipping a glass electrode into it with a digital pH metre. The pH of each formulation was measured three times and the average value was calculated.

**3. Spreadability:** The diameter of the emulgel circle formed when the emulgel is sandwiched between two equal-weight glass plates. On one glass plate, a weighed amount of emulgel (350 mg) is placed, and another glass plate is dropped from a distance of 5 cm. The spread emulgel circle's diameter is measured.

The formula  $S=M$  is used to calculate it.



L/T where S denotes spreadability

M denotes a weight attached to the upper slide.

L is the length of the glass slide.

T denotes the amount of time required to completely separate the slides.

**4. Extrudability Study [tube test]:** It is calculated using the force required to extrude the emulgel from the tube. The method for determining applied shear in the region of the rheogram with a shear rate greater than the yield value and plug flow. In this study, emulgel was extruded from a lacquered aluminium collapsible tube at the weight in grammes required to extrude at least a 0.5cm ribbon of emulgel in 10 seconds. More material is extruded to improve extrudability. The extrudability is measured three times and the average values are computed. The formula below is then used to calculate the extrudability.

Extrudability = weight used to extrude emulgel from tube (in gm) / surface area (in cm<sup>2</sup>).

**5. Rheological Studies:** At 25°C, the viscosity of the emulgel is measured using a cone and plate viscometer with spindle 52 and a thermostatically controlled circulating water bath.

**6. Swelling Index:** in a 50ml beaker, combine 1g of emulgel in a porous aluminium foil with 0.1N NaOH. The samples are then removed at regular intervals and dried before being reweighed. The swelling index is calculated in the following way:

$$W_t - W_0 / W_0 \times 100 = \text{Swelling Index}$$

Where (SW) percent is the equilibrium percent swelling,

W<sub>t</sub> is the weight of the swollen emulgel after time 't',

W<sub>0</sub> is the weight of the emulgel at zero time.

**7. Drug Content Determination-** Emulgel is dissolved in an appropriate solvent. Filter the solution to get a clear one. Determine its absorbance using a UV spectrophotometer. The standard equation can be used to calculate the absorbance value, concentration, and drug content. Conversion Rate = (Concentration Dilution Factor Volume Taken)

#### **8. Testing for bioadhesive strength-**

The modified method was used to assess bioadhesive strength. The apparatus consists of two arm balances, with both ends strung to glass plates. One side has a single weighing glass plate. The right and left pans were balanced by adding weight to the left pan. The balance was held in this position for 5 mints.

#### **Procedure:**

Extra weight from the left pan was removed to sandwich the two pieces of glass, and some pressure was applied to remove the presence of air. For 5 minutes, the balance was held in place. Weight was gradually added to the left pan at a rate of 200mg/min until the two glass slides separated. A formula is used to calculate bioadhesive strength by using the weight required to detach the emulgel from the glass surface.

$$\text{Bioadhesive strength} = \text{weight required (in g)} / \text{area (cm}^2\text{)}$$

**9. Skin Irritation Test (Patch Test):** In this study, an emulgel is applied to a rat's shaved skin, and the adverse effects, such as colour change and skin morphology, are monitored for up to 24 hours. The experiment can use up to eight rats. The test is considered successful if there is no irritation. If the test is unsuccessful, it is repeated with two more rats.

**10. Microbiological assay:** The microbiological assay was performed using the ditch plate technique. The previously prepared Sabouraud's agar dried plates were used. 3 grammes of gellified emulsion are placed in a ditch cut in a plate. Freshly prepared culture loops are streaked across the agar plate at an angle. After 18-24 hours of incubation at 25 degrees Celsius, fungal growth was observed and the percentage inhibition was calculated.

**11. In vitro diffusion studies:** A diffusion study of a prepared emulgel is demonstrated using a Franz diffusion cell. 0.5g of sample is spread on a cellophane membrane during the study, and diffusion is carried out for 8 hours at 37°C using phosphate buffer (pH 7.4). A 1 ml sample is collected after 1 hour and replaced with fresh buffer solution. An appropriate analytical method is used to analyse the collected samples.

**12. Accelerated stability studies:** The formulations are stored in ovens at 37°C, 45°C, and 60°C for three months in accordance with ICH guidelines. The drug content is tested every two weeks using an appropriate analytical method. Stability is determined by the change in pH of the gel or the degradation of the drug.

## **II. CONCLUSION**

Emulgel is a cutting-edge tool for the topical administration of hydrophobic drugs that

combines the advantages of emulsion and gel to improve patient acceptability. Spreadability, adhesion, viscosity, and extrusion are all improved by emulgel. It is used in both pharmaceutical and cosmetic applications, and it allows herbal formulations to be included.

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