A Review on Emulgel – A Novel Trend in Topical Drug Delivery

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Abstract:

Topical drug delivery systems have long been employed to treat localized skin conditions while minimizing systemic side effects. Among the advanced approaches, emulgel has emerged as a promising hybrid formulation that integrates the properties of emulsions and gels. This review provides a comprehensive overview of emulgels, highlighting their formulation principles, preparation processes, and evaluation parameters. Key formulation components like oils, emulsifiers, gelling agents, humectants, antioxidants, and preservatives are analyzed for their role in stability, drug release, and patient acceptability. Special attention is given to microemulgels and nanoemulgels, which offer enhanced penetration, controlled release, and improved therapeutic efficacy compared to conventional topical systems. Evaluation techniques such as rheological studies, drug release kinetics, entrapment efficiency, and microbiological assays are outlined to ensure product quality and reproducibility. By addressing limitations of creams, ointments, and gels, emulgels provide superior spreadability, bioavailability, and patient compliance. Overall, emulgels represent a novel and versatile platform for delivering both hydrophilic and hydrophobic drugs, with significant potential in dermatology, cosmetics, and pharmaceutical applications.

Key words: Topical drug delivery, Nanoemulgel, Controlled release, Gelling agents, Patient compliance, Emulsion, Microemulgel.

I. Introduction:

A topical drug delivery system is a method of administering medication through the skin to provide a topical therapeutic effect. Topical drug delivery systems are used when other routes (such as oral, sublingual, parenteral, or rectal) fail to treat local skin infections, such as fungal infections. Topical medications' main benefit is their ability to avoid presystemic metabolism.[1]

Directly treating cutaneous conditions by putting a drug-containing formulation to the skin is known as topical medicine delivery. Topically administered medications can either act at the application site or have systemic effects. The skin absorbs drugs more readily when they are in solution, have a favourable lipid/water partition coefficient, and are non-electrolytes.[2]

Emulgel has gained popularity as a topical semisolid dose form since the 1980s[1]. Emulsion gels, sometimes referred to as emulgels, emulsion hydrogels, or emulsion-filled gels, have garnered increasing attention lately because of their qualities, which make them useful in a variety of sectors, including food, cosmetics, and pharmaceuticals.[3]

The term "emulgel" refers to gelled emulsions, which are created by adding a gelling agent and can be either water-in-oil or oil-in-water. Compared to alternative topical preparations, emulgels are more stable.[4]

II. Physiology of Skin:

A typical adult's skin has a surface area of around two meters square and receives about one-third of all blood circulations. It is one of the largest and easiest-to-reach organs on the human body, and it is only a few millimetres thick. The skin acts as a barrier against physical, chemical, and microbiological threats and isolates the underlying blood circulation network from the external environment.

The skin is a complex organ made up of numerous layers. In general, the epidermis, dermis, and hypodermis are the three main layers that are described. Under a microscope, the dermis is further separated into five anatomical layers, with the stratum corneum serving as the outermost layer of the epidermis that is exposed to the outside world. The Statum Corneum is made up of several layers of keratinized, compacted, dried cells.

Dermatological medications have been administered topically for many years in order to produce a localized pharmacological effect on the skin tissue. Before being released into the bloodstream for excretion, the drug molecule in this instance is thought to diffuse to a specific tissue close to the site of drug application to have its therapeutic action.[5]

A. Epidermis:

The epidermis is avascular, meaning it lacks blood vessels, and it is between 0.5 and 1.5 mm thick. "Thick skin" refers to the skin on the palms, soles, and fingerprints, whereas "thin skin" refers to the skin on other parts of the body. The stratum corneum, stratum granulosum, stratum spinosum, also known as the prickle cell layer, and stratum germinativum (also known as the stratum Basale), are the four epithelial layers that make up the epidermis of thin skin.[6]

- **Stratum basale (Base layer):**

Columnar cells form a single layer in the stratum Basale. Only cells in the epithelium's deepest stratum undergo mitosis. This regeneration process causes cells to migrate or transfer from the base layer through the other layer until they are removed from the skin's surface.

- **Stratum spinosum (Spiny layer):**

The epidemic's stratum spinosum, or "spiny layer," is made up of eight to ten layers of asymmetrically structured cells with noticeable desmosomes or intercellular bridges. It is common to refer to the stratum Basale and the stratum spinosum together as the stratum germinativum (growth layer). Sometimes anatomists just refer to the basal layer of cells by this designation.

- **Stratum granulosum (Granular layer):**

The epidemic's stratum granulosum is where the surface keratin formation process starts. Cells are layered two to four deep and contain kerato-hyalin, a highly staining substance necessary for the formation of surface keratin.

- **Stratum lucidum (Clear layer):**

The stratum lucidum contains transparent, flat keratinocytes that are densely packed. Usually, there are no nuclei and the cell edges are now clearly visible. Eleidin is a material found inside these dying cells that will eventually change into keratin.

- **Stratum corneum (Horny layer):**

The epidermis's outermost layer is called the Statum Corneum. It is made up of extremely thin, flat, squamous cells that are constantly being shed and replaced near the skin's surface. Because it acts as a barrier against water loss and a variety of environmental dangers, including bacteria, dangerous chemicals, and physical damage, the stratum corneum is sometimes referred to as the skin's barrier area.[7]

B. Dermis:

Depending on the exact spot of the skin, the dermis can range in thickness from less than 0.5 mm to over 5 mm. Collagen and elastic tissue are the two main forms of protein fiber. collagen is the most abundant extracellular matrix protein in the dermis, according for 80-85% of its dry weight

There is a highly rich blood supply in the dermis, even though no vessels cross the dermal–epidermal junction.[8]

C. Hypodermis:

The main component of the hypodermis is loose connective tissue, which can form gliding layers or massive pockets of adipose tissue that shield and insulate the skin depending on the area.
Proteoglycans and glycosaminoglycans, which are quite common in the tissue, pull fluid into it and make it feel like mucus. The cell types that comprise the hypodermis are macrophages, adipose cells, and fibroblasts. They have a particular function in preserving adipocyte homeostasis in obesity, may be connected to tissue remodeling, and may encourage fat thermogenesis in response to cold and exercise. The "microvacuolar" tissue of the hypodermis functions as an active reservoir of interstitial fluid, capable of dynamically altering the structural rigidity of the tissue.[9]

III. Gels:

Gels are a new type of dosage form that are made by trapping large amounts of aqueous or hydroalcoholic liquid in a network of colloidal solid particles.

These particles can be inorganic substances like aluminum salts or organic polymers that are synthetic or natural. They contain a greater amount of aqueous material than ointment or cream bases, which facilitates better drug solubility and simpler drug migration via a vehicle.

These are better in terms of patient acceptability and ease of usage. Despite gels' many benefits, one significant drawback is their inability to administer hydrophobic medications. Emulgels are made and used to overcome this restriction, allowing even a hydrophobic medicinal moiety to benefit from the special qualities of gels.[10]

IV. Emulgel:

Emulsions are colloidal dispersion systems in which two immiscible liquids are stabilized by an emulsifier, causing minute droplets of one liquid to disperse throughout the other.[11]

An emulgel is a dosage form that combines emulsions with gels. It is an excellent formulation that combines the benefits of a gel with an emulsion. These benefits include the ability to incorporate both hydrophilic and hydrophobic medications, allow for controlled drug release,

enhance stability, lower production costs, and increase aesthetic appeal due to their emol lient, thixotropic, easily spreadable, bio-friendly, non-greasy, and non-staining properties.[12]

Emulgels consist of emulsions, either water-in-oil or oil-in-water, that are gelled by combining them with a gelling agent. Drug particles trapped in the internal phase of an emulsion travel through the exterior phase to the skin, where they are gradually absorbed, making it a controlled release mechanism. Gel forms a cross-linked network that captures and releases small medicine particles in a regulated manner. Its mucoadhesive properties enable it to adhere to the skin for an extended period of time. Emulgel combines the properties of gel and emulsions to operate as a dual control release device. For emollient and dry skin treatments, water-in-oil emulsions are more commonly utilized, whereas oil-in-water emulsions work better as water-washable drug bases and for general cosmetic purposes.[13]

Among the essential features of Emulgels are:

a) Hydrophilic-lipophilic balance (HLB): The emulsifiers' HLB determines whether an oil-in-water or water-in-oil emulsion forms.
b) Viscosity: Gives an Emulgel-like consistency and keeps phases from separating. This is achieved with aqueous phase thickeners.
c) pH: The compounds that are used determine the pH of Emulgels, which affects drug stability, skin irritation, and penetration. The majority of emulgels have a pH between 5 and 8.
d) Spreadability: For easy application and active release, Emulgels need to have a smooth, spreadable consistency.[14]

V. Formulation components of Emulgel:

A. Vehicle:

Both hydrophobic and hydrophilic medications are used in the emulgel formulation, along with aqueous and oily solvents. Aqueous phase emulsions use a variety of solvents, including water, alcohol, and other aqueous substances.[15]

B. Oils:

When choosing a substance for the oil phase of an emulsion that is employed to make hydrophobic pharmaceuticals soluble, its effects on viscosity, permeability, drug release, emulsification, and stability are optimized. Since different oils have therapeutic potential, it can also be chosen based on the effect of the active chemical that produces the synergistic effect. Mineral oils, propylene glycol, liquid paraffin, wool wax, soybean oil, cottonseed oil, oleic acid, and so on are the most often used oil phases.[16]

The pharmaceutical industry frequently uses natural oils as an emollient, therapeutic enhancer, or delivery system for hydrophobic medications, whether in their natural state or in emulsion formulations. Many oils, like andiroba oil and sweet almond oil, help to prevent damage at different phases of skin recovery.[17]

C. Emulsifiers:

The emulsifying agents have the primary responsibility for reducing the interfacial tension that enhances the stability of the emulsion. An emulsion that is stable and has a sufficient Hydrophilic-Lipophilic Balance (HLB) should be produced by the specified emulsifying agent.

Additionally, the stability of the emulsion is strongly correlated with the type and quantity of emulsifying agent used to form it. Typically, w/o emulsions are made with emulsifying agents that have an HLB of less than 8, whereas o/w emulsions are made with those that have an HLB of more than 8. The purpose of emulsifying chemicals is to maintain stability over the course of the shelf life and to encourage emulsification during production. Stearic acid, sodium stearate, sorbitan monooleate (Span 80), and polyoxyethylene sorbitan monooleate (Tween 80) are examples of common emulsifier.[18]

D. Gelling agent:

By combining emulsion to create an emulgel, gelling agents are utilized to create a gel base. These substances, commonly referred to as thickening agents, increase the consistency of any dosage form by creating a jelly-like structure and swelling in the aqueous phase. A system becomes thixotropic when a gelling agent is added. Because it demonstrated a higher drug release rate, HPMC-based Emulgel was determined to be superior to Carbopol-based Emulgel. For vaginal application, NaCMC-based emulgels demonstrated superior in-vitro and in-vivo performance along with better mucoadhesiveness, which extended drug residence time. Emulgel based on HEC demonstrated good rheological and drug release profiles, but little mucoadhesion. Emulgel with a pemulen basis was intended for buccal administration.[16]

E. pH adjusting Agent:

These substances are employed to keep the formulation's pH stable. Such as NaOH, triethylamine, etc.[15]

F. Preservatives:

Preservatives are chemicals that are frequently added to a variety of foods and medications to increase their shelf life. Preservatives must be added to these items, particularly those with a greater water content, to prevent microbial alterations and degradation while they are being stored.[19]

To prevent microorganisms from spoiling the formulation, preservatives are added to emulgel and are used to stop the growth of microorganisms. This includes benzoalkonium chloride, benzoic acid, benzoyl alcohol, propyl paraben, and methyl paraben.[20]

G. Antioxidants:

Nowadays, antioxidants are employed as effective excipients that slow down or stop molecules from oxidizing[21]. The emulgels' usage of antioxidants improves the medicinal ingredients' stability, like BHA, BHT, etc.[20]

H. **Humectant**:

Humectants are organic compounds that are hygroscopic and have the ability to absorb and retain water, which improves the texture and softness of foods and medications. Furthermore, the majority of the hydrophilic groups found in humectant molecules are hydroxyl groups [22]. The purpose of the humectant is to keep the emulgel compositions wet. Humectants that are frequently utilized are glycerine and propylene glycol.[20]

VI. Factors affecting the release:

The release of active drugs is affected by factors like,

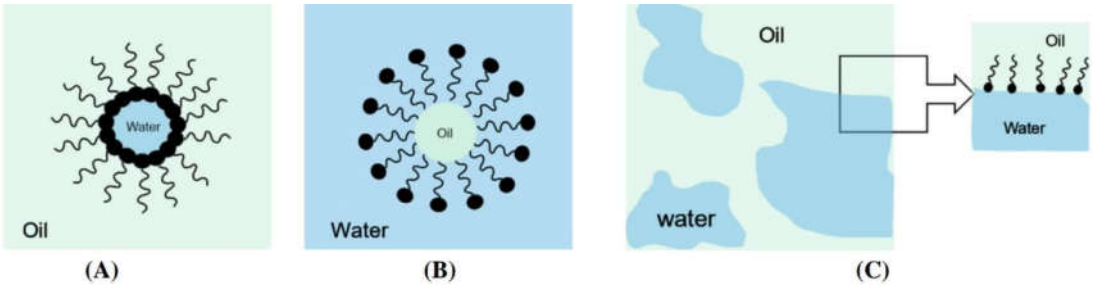
- API (concentration & physio chemical properties)
- The size of the particles
- The surfactants concentration and the type of surfactants used
- The polymers concentration and the type of polymers used
- Which type of penetration enhancers are used
- The factors of physiological.[23]

VII. Types of Emulgel:

1. Microemulsion based Gels:

Hoar and Schulman first proposed the idea of a microemulsion in the 1940s. Microemulsion, a colloidal system, is a significant delivery vehicle for lipophilic and hydrophilic medicines due to its unique qualities, which include translucent, optically isotropic, thermodynamically stable nano-sized droplets and penetration due to its very low surface tension. An oil phase, an aqueous phase, a surfactant, and a co-surfactant self-assemble to form a well-defined, thermodynamically stable system known as a microemulsion. The microemulsion is uniformly dispersed and has droplets ranging in size from 10 to 100 nm. For topical and transdermal formulations, microemulsions offer a number of benefits, such as enhanced skin penetration rates and better skin delivery through the increased solubility of hydrophilic and lipophilic molecules.

Microemulsion systems can be categorized into water-in-oil (w/o) and oil-in water (o/w) varieties, or bi-continuous (BC) structures, in which the two phases coexist without forming discrete spherical droplets.



Microstructures of the microemulsion

A. Water in oil microemulsion, B. Oil in water microemulsion, C. Bi-continuous microemulsion

Advantages of Microemulsion based system:

As a drug delivery method, microemulsions provide a number of benefits.

1. A large loading capacity.
2. The sustainability of production.
3. The ability to integrate hydrophobic medications.
4. No vigorous sonication.
5. Prevents the first-pass effect.

6. Implemented controlled release.

Disadvantages of Microemulsion based system:

1. Need a lot of surfactant or co-surfactant to keep droplets stable.
2. A surfactant used in pharmaceutical applications needs to be harmless.
3. Environmental factors like pH and temperature have an impact on microemulsion stability.[2]

2. Nano-Emulsions based Gels:

The term "nano-emulsions" (NEs) refers to a mixture of two immiscible liquid phases stabilized by surfactants in the form of 200–300 nanometer-sized nano-droplets, usually of the oil-in-water kind. Despite having some traits in common with macro-emulsions, like thermodynamic instability and adaptability (like organoleptic and rheological properties), NEs also have some distinct features due to their range of nanometric sizes, such as optical clarity, superior stability, and a large surface area.[25] Extremely tiny dispersed phase droplet sizes, usually ranging from 10 to 100 nm, characterize nano emulsions (NEs). There is no clear restriction on this range of droplet sizes because other articles report droplet sizes of less than 100 nm (pharmaceuticals), 20 to 200 nm, 10 to 200 nm, 50 to 200 nm, and 50 to 1000 nm.
They have stability against sedimentation and creaming and are visible to the naked eye as transparent or translucent, even at large droplet volume fractions. Other names for NEs include sub-micron emulsion, ultrafine emulsion, and mini-emulsion. NEs differ from the other forms of emulsions in a number of physical characteristics.

Advantages:

The small droplet size of NEs results in excellent kinetic stability, large interfacial area, and optical transparency, making them superior to traditional emulsions (micrometer-size droplets). Because of their small size, Brownian motion overcomes gravity, making NEs stable to sedimentation or creaming. However, they can also experience flocculation, coalescence, and Ostwald ripening.[26]

3. Macroemulsion Gel:

Emulgel with emulsion droplets larger than 400 nm. Despite their outward invisibility, the individual droplets are readily visible under a microscope. Despite their thermodynamic instability, macroemulsions can be stabilized with the use of surface-active chemicals.[15]

Differences in Nanoemulgels (NEs) and Microemulgel (MEs):

The differentiations between the two types of Emulgels are given below.[25]

S NO	NANOEMULGELS (NEs)	MICROEMULGEL (MEs)
1	Since the colloidal system's Gibbs energy is higher than that of the water and oil phases, it is proposed that the growth of NE is energetically unfavourable. So, NE can be produced only with external energy.	It is easy to form oil and water phases because their Gibbs energy is higher than that of colloidal systems.

2	It is thermodynamically unstable	It is stable
3	Capable of loading a sufficient quantity of dispersed phase.	Capable of loading a large quantity of dispersed phase.
4	The ratio of surfactant oil ranges from 1 to 2.	The ratio of surfactant oil must be more than two.
5	Many different types of surfactants can be employed.	Only small molecule surfactants are suitable.
6	The particle is primarily spherical in form	Shapes can be either spherical or non-spherical (worm-like, cylinder, spheroids, etc.).

VIII. Preparation process of Emulgel:

There are mainly 3 steps followed to prepare an Emulgel.

1. Emulsion formulation, either O/W or W/O.
2. Gel base formulation.
3. Incorporate the emulsion into the gel base while stirring continuously.[27]

1. Emulsion Formulation, Either O/W Or W/O:

The initial step in the construction of an emulsion is the dissolution of water-soluble elements in an aqueous vehicle (such as tween 80 in filtered water) and oil-soluble materials in an oil vehicle (such as span 20 in liquid paraffin. Both phases were mixed in turbulent mixing conditions to guarantee that they would disperse into droplets. While industrial manufacturing emulsification is often carried out using mechanical stirrers, ultrasonifers, homogenizers, or colloid mills, laboratory emulsion preparation uses a mechanical stirrer.[28]

2. Gel Base Formulation:

Gelling agents (thickening agents) are substances that improves the consistency of any dosage form. In order to make gel, the polymer is often chosen depending on the external phase's characteristics.[29]

The first step involves utilizing mechanical stirring in a mixing vessel to dissolve the water-soluble materials, also known as excipients, in the aqueous vehicle. To avoid aggregation, the hydrophilic polymer is added gradually to the agitated mixture while stirring continuously until the polymer dissolves and the pH remains within an acceptable range. The rate of mixing must be reasonable since excessive stirring of pharmaceutical gels can cause air to become trapped.[28]

3. Incorporate the Emulsion into the Gel base while stirring continuously:

Emulgel is made by gradually adding the prepared emulsion to the gel base while continuously stirring with a homogenizer.[30]

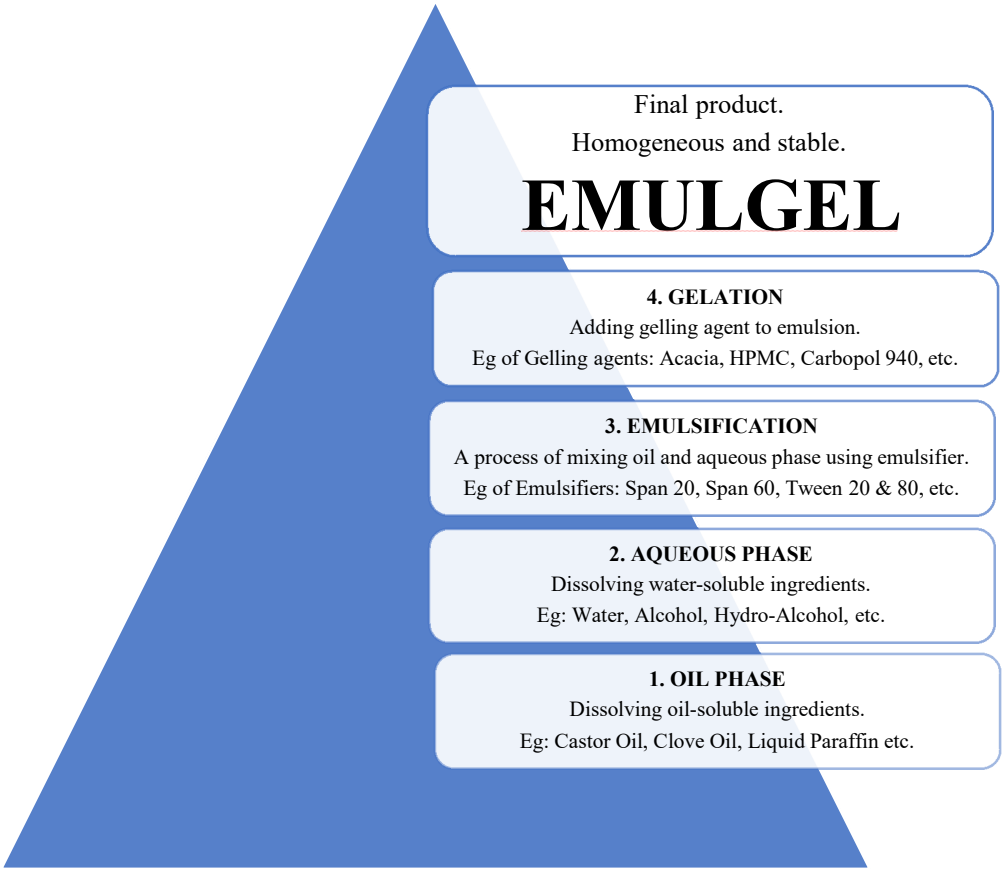
An additional method for producing Emulgel.

There are three primary steps involved:

1. Making the oil phase emulsified.
2. The polymeric aqueous dispersion is neutralized, and
3. In water, the polymer is dispersed.

Stirring for 20 minutes at 900 rpm disperses the polymer. The sodium hydroxide solution is then used to neutralize the produced slurry, resulting in a clear and stable gel. The polymer is subsequently treated to complete hydration of gel.[31]

Steps involved in preparing Emulgels:[29]



IX. Evaluation of Emulgels:

1. **Physical Appearance:**

The emulgels' color, homogeneity, consistency, and pH were examined visually.[32]

2. **pH:**

The pH values of each developed formulation ranged from 5.4 to 6.4, which is suitable for avoiding skin irritation because the average pH of adult skin is around 5.5.[33] The formulation's pH was measured using a digital pH meter; the electrode was washed with distilled water before being submerged in the mixture.[34]

3. Particle size distribution (PSD):

In order to avoid droplet aggregation, samples were diluted with distilled water at a weight ratio of 1:20 for emulgels containing 20% w/w of oil and 1:30 for emulgels containing 30% w/w of oil. The samples were then gradually mixed using a magnetic stirrer so as not to change the droplet distribution. The PSD of emulgels was measured with a contrast phase optical microscope. After a drop of diluted emulgel was applied to the microscope slide, the images were examined using an integrated micro-camera (Dhs Micro-cam3.1, Germany). Data from the image processing program Dhs Particle Analysis (dhs image database, Germany) were statistically analyzed to produce the PSD. The particles were colored in order to determine their comparable circular area diameter.[35]

4. Spreadability:

The property known as spreadability is used to describe how much of the skin a formulation can readily cover when applied topically. According to Al-Suwayeh et al., the spreadability value of emulgel influences its therapeutic efficacy. According to Mishra et al., emulgel's spreadability is also a key component in improving patient compliance since a formulation with a high spreadability value allows for more comfortable and consistent administration across skin that is irritated.[37] The viscosity of emulgel determines its spreadability. The time required for spreading will increase with increasing viscosity. After placing 500 mg of emulgel in a weighed quality on one glass plate, another glass plate is placed five centimeters away. The circle's spread emulgel diameter is measured.[34]

5. Skin Irritation Study:

If the active ingredients are left on the skin for an extended period of time after application, they may cause irritation. Therefore, it is crucial to assess how the formulation and skin interact in terms of skin sensitivity. Both the test group (emulgel) and the control group (placebo) had their skin irritation symptoms (erythema and edema) monitored for three days.[36] The experiments on skin irritation were conducted on guinea pigs. One day prior to the trial, the guinea pigs' dorsal skin area was shaved with a clipper. After three days of treatment with test formulations, the animals' skin was visually inspected for signs of edema and erythema. The untreated skin, which served as a control, was compared to the observations.[37]

6. Rheological Studies:

The viscosity of the various emulgel formulations was assessed at 25°C using a thermostatically controlled circulating water bath (Polyscience, model 9101, Niles, IL) connected to a cone and plate viscometer with spindle 52 (Brookfield Engineering Laboratories, model HADV-II, Middleboro, MA). The recorded viscosities are listed in a table.[38]

7. Stability Study:

One crucial factor that affects the consistency, therapeutic effectiveness, and quality of a pharmacological product under various pH, humidity, and temperature storage conditions is formulation stability. The improved emulgel was evaluated for color, phase separation, smell, homogeneity, and grittiness after being stored under different conditions for a shorter period of time.[36]

8. Microbiological Assay:

It was done using the ditch plate technique. It is a technique for evaluating the bacteriostatic or fungistatic activity of a substance. Typically, semisolid formulations are utilized. The previously made Sabouraud's agar dried plates were utilized. Three grams of the emulgel were put to a ditch made in the plate. Newly created culture loops were streaked at a right angle across the agar from the ditch to the edge of the plate. Commercial CHL powder was used as a comparison. Control plates were also created using basic emulgel bases. The fungal growth was evaluated after 18 to 24 hours of incubation at 25°C, and the percentage inhibition was computed using the formula,

$$\% \text{ inhibition} = \frac{L2}{L1} \times 100$$

Where, L2 is the inhibitory length, while L1 is the streaking culture's overall length.[38]

9. Invitro Drug Release:

Franz diffusion cells were used to measure the invitro drug release using membranes of mixed cellulose esters type Millipore HA 0.45 μm (membrane surface area of 3.14 cm2). Thirty minutes prior to the samples being placed, synthetic membranes were exposed to phosphate-buffered saline (PBS; pH 7.4). The receptor fluid had a capacity of 15 ml, and sink conditions were achieved in the receptor compartment using PBS. A swirling magnetic bar was used to continually homogenize the receptor compartment during the experiment. A water circulation system was used to maintain the temperature at 32°C (28–30). Experiments were conducted with a dose of 500±10mg ("infinite dose"; n=3) to replicate consumption conditions. On the membranes, the preparations were dispersed equally. Five milliliters of PBS receptor fluid were used for the UV concentration measurement at nm. After 0.5, 1, 2, 4, and 6 hours, serial sampling was performed, and fresh receptor liquid was supplied to the receptor compartment to restock the buffer.[39]

10. Drug content determination:

Two distinct techniques were created and tested in the lab to ascertain the drug content of the emulgels: one for emulgels made with non-ionic surfactants and another for those made with cationic and anionic surfactants. Using 0.1 M HCl as the solvent, the emulgel made with Span 20 and Tween 20 was examined. One gram of produced emulgel, precisely weighed, was dissolved in 0.1 M HCl solution. After further diluting this dispersion with 0.1 M HCl, a UV spectrophotometer was used for analysis.

To determine the drug content in emulgels made with cetrimide and SLS, the following technique was used. The first stage involved dissolving 500 mg of precisely weighed emulgel in dichloromethane and shaking it for two hours. After filtering, the solution was moved to a watch glass. Heating the solution on the watch glass caused the dichloromethane to evaporate, leaving the residue behind. The residue was assessed using a UV spectrophotometer with the addition of 10 milliliters of methanol and further dilution with phosphate buffer pH 7.4.[37]

11. Drug release kinetics studies:

The following release models: zero order, first order, and Higuchi model, were identified by kinetic analysis of the data. These models explain the correct order of drug release.[41]

The zero order plots were made by graphing the cumulative percentage of drug penetrated on the vertical axis versus time (in hours) on the horizontal axis. To check the formulations for first order kinetics, the log cumulative % medication remaining was plotted versus time (in hours). Furthermore, the square root of time (in hours) on the X-axis and the cumulative percent medication permeated taken on the Y-axis were compared to create the Higuchi plots. The best model was found using the goodness-of-fit test. It was believed that the plot with the highest correlation coefficient (r2) value was the most appropriate for the particular formulation.[37]

12. Swelling index:

Place 1g of emulgel in a 50ml beaker with porous aluminum foil and dip it in 0.1N NaOH. Samples are taken out, allowed to dry, and then weighed again at various intervals. The calculation of the swelling index is as follows:

$$\text{Swelling Index} = \frac{Wt - Wo}{Wo} \times 100$$ [34]

13. Entrapment efficiency:

The fraction of the drug quantity that is entrapped in the formulation is known as entrapment efficiency. To verify the efficacy of the entrapment, the unentrapped medication was separated by centrifugation for 30 minutes at 15,000 RPM. Both the liquid supernatant and the resulting solution were collected. After being diluted with suitable solvent (methanol), the recovered supernatants were measured using specified instruments.[41]

X. Advantages of Emulgel:

1.Emulgel avoids First pass metabolism.[42]

2.It offers better patient compliance.[31]

3.With a shorter $t_{1/2}$, Emulgels can be utilized to extend the duration of the drug's impact (controlled release).[43]

4. These formulations have the benefit of acting specifically in the intended location.[44]

5.It Avoids the incompatibility with the stomach.

6.Drugs which are incorporated into the Emulgel have a short biological half-life and a restricted therapeutic window.

7.This delivery system offers someone (Patients) to stop taking medication as soon as needed.[45]

8.Phase inversion is the main issue with topically applied creams, whereas hygroscopic nature is the main issue with topical powders. Emulgel is preferable to other conventional topical preparations because it does not have this issue.

9.The major benefit of emulgel is its ability to effortlessly transport lipophilic medications by combining them with gel-based drug-oil-in-water emulsion. Solubility is the main obstacle that prevents lipophilic medications from being released into the systemic circulation when they are directly incorporated into gel. By combining the advantages of gel and emulsion in a single formulation, the Emulgel enhances the stability and drug release profile of the lipophilic medication.

10. Emulgels have a longer shelf life and are the most stable topical preparation when compared to the other formulations. [31]

11. Extensive ultrasound treatment is necessary for the creation of vesicular particles, which may cause medication leakage and degradation. However, since ultrasound treatment is not necessary, this issue does not occur during the emulsion production process. [43]

12. Emulgel's loading capacity is higher than that of the other topical treatments. Because the entrapment efficacy of topical preparations based on nanoparticles is limited. Emulgel's loading capacity is also greater than that of innovative niosome and liposome-based preparations.[31]

13. Emulgel preparation increases production viability by requiring only a few simple steps.[44]

XI. Disadvantages of Emulgel:

1. Certain medications only enter the skin partially.[45]

2. Small bubbles may occasionally form in Emulgel, which decreases the drug's penetration into skin.[31]

3. The potential for allergic responses.[46]

4. Contact dermatitis-induced skin irritation.[47]

5. It is difficult for drugs with large particles size to pass through the skin.[48]

XII. Future Prospectives:

A frequent problem encountered during the development and implementation of any novel dosage form is the aquaphobic behaviour of pharmaceuticals, which ultimately results in poor aqueous solubility and pharmacokinetic issues. Since many medications are aquaphobic, administering them to the biological process has proven difficult. Moisturizers, lotions, and various cosmetic preparations are examples of medicine delivery methods that have been applied topically. They have good demulcent properties but slow drug release because they contain oily bases such petroleum jelly, honey waxes, or vegetable oils, which are aquaphobic and prevent the addition of an aqueous phase.

Compared to some other topical drug delivery system (TDDS) techniques, the gel promotes faster medication release by giving medications an aqueous environment. It is possible to combine hydrophobic medications with greasy bases and apply them topically using emulgel. Emulgel is more successful and profitable than other topical pharmaceutical delivery systems because of all these benefits. These characteristics will be applied in the future to a wider variety of topical medications, including emulgel.[49] Emulgel is a relatively recent topical drug delivery technique that is effective with drugs that are aquaphobic.[50]

XIII. Literature Review:

S No	Drug Name	Objective of the study	Oil Used	Gelling Agent Used	Type of Emulgel	Category	References
1	Diclofenac	To formulate and evaluate a stable diclofenac emulgel using natural permeation enhancers for enhanced drug release, bioavailability and skin penetration	Liquid paraffin	Carbopol 934 and HPMC	Oil in water emulgel	Topical treatment osteoarthritis and rheumatic pain	Nalik et al., 2025. (33)
2	Meloxicam	To formulate and evaluate meloxicam emulgel for topical treatment of pain and inflammation, enhancing permeability and patient compliance	Liquid paraffin	Carbopol 974	Oil-in-water (O/W) emulgel	Non-steroidal anti-inflammatory drug (NSAID)	Mahmoud Mahyoob Alburyhi et al.,2025. (63)
3	Phycocyan	To evaluate Phycocyanin as a natural stabilizer and its combinations with	Avocado Oil	Diutan Gum	Protein-Polysaccharide emulgel	Antioxidant and Anti-inflammatory potential.	Tello etal., 2024. (11)

		Diutan gum to develop stable biocompatible emojis for potential food and biomedical applications.					
4	fluconazole	Formulate flu conazole for vaginal applications	Palm Olein	Xanthan gum or HPMC E5LV	Emulgel	Vaginal Candidiasis	Ogedengbe & kolawole, 2024. (52)
5	Eugenia caryophyllus (Clove) Buds Extract	To formulate and evaluate clove buds extract emulgel for antibacterial and anti-inflammatory activity	Essential oil of clove, paraffin liquid, oleic acid	Carbopol 940	Oil-in-water (O/W) emulgel	Antibacterial and anti-inflammatory herbal formulation	Jubershaha S. Fakir et al.,2024. (59)
6	Markhamia tomentosa leaf extract	To develop and characterize an emulgel formulation of M. tomentosa and evaluate its antimicrobial activity against skin isolates	Liquid paraffin	Carbopol 934	Oil-in-water (O/W)	Antimicrobial / Herbal	Oseni, B., et al., (2024). (65)
7	Ketoconazole	To develop and evaluate ketoconaz	Oleic acid	Carbopol 934	Nano emulgel	Dermatophyte infection	Harde et al., 2023. (41)

		ole nanoemulgel using 3^2 factorial designs					
8	Dasatinib	To design and optimize dasatinib nanoemulgel using QbD and evaluate anti-inflammatory activity	Peceol + Geleol	Carbopol ETD 2020	Nanoemulgel	Rheumatoid arthritis	Donthi et al., 2023. (51)
9	Naproxen+ eugenole	To co-load naproxen and eugenol in emulgel for synergistic analgesic and anti-inflammatory effects	Not specified (likely light paraffin or essential oils)	Sepineo P600 & carbopol	Transdermal emulgel	Pain and inflammation	Khan et al., 2022. (36)
10	Fluconazole	To formulate and evaluate a topical emulgel of fluconazole using jojoba oil and liquid paraffin, optimized via Central Composite Design for antifungal therapy	Jojoba oil, Liquid paraffin	Carbopol 940	Oil-in-water emulsion gel (emulgel)	Topical antifungal drug delivery	Kumar et al.,2022. (29)
11	Imiquimod	To develop and optimize an emulgel system for	Light liquid paraffin	Carbopol 934, Carbopol 940	Oil-in-water (O/W)	Antiviral / Immunomodulator	Arti Prajapat, et al., 2022. (66)

		topical delivery of Imiquimod to treat common warts with better drug release and skin penetration than marketed products					
12	Malus domestica Borkh (Apple extract)	To formulate gels and emulgels containing phenolic-rich apple extracts and evaluate their antioxidant activity and biopharmaceutical properties in vitro	Castor oil	Carbomer 980	Oil-in-water (O/W)	Antioxidant / Dermatological	Aurita Butkeviciute, et al., 2022. (68)
13	Meloxicam	To formulate and evaluate meloxicam emulgels (including fixed dose with a capsaicin) as a safe and effective tropical alternative for managing rheumatic conditions	Liquid Paraffin	Carbopol-934	Oil-in-Water emulgel	Topical Treatment of rheumatism	Mwangi et al., 2021. (12)

14	Propolis (PRP)	To evaluate the effect of different vegetable oils and poly (acrylic acid) derivatives on the physicochemical, mechanical, and rheological properties of emulgels for topical delivery	Sweet almond oil (SA), Andiroba oil (AN), Passion fruit oil (PF)	Carbopol 934P®, Carbopol 974P®, Polycarbophil (PC)	Oil-in-water emulsion gel (emulgel)	Topical drug delivery system	Said dos Santos, R. et al., 2021. (17)
15	Curcumin (CUR)	To evaluate the effect of different vegetable oils and poly (acrylic acid) derivatives on the physicochemical, mechanical, and rheological properties of emulgels for topical delivery (co-delivered with PRP or alone)	weet almond oil (SA), Andiroba oil (AN), Passion fruit oil (PF)	Carbopol 934P®, Carbopol 974P®, Polycarbophil (PC)	Oil-in-water emulsion gel (emulgel)	Topical drug delivery system	Said dos Santos, R. et al., 2021. (17)
16	Celecoxib	To formulate and evaluate	Liquid paraffin	Carbopol 934 and	Oil-in-water (O/W) emulgel	Non-steroidal anti-inflammat	M. Sunitha Reddy et al.,2020. (56)

		celecoxib emulgel using Carbopol 934 and 974 for enhanced topical delivery and diffusion efficiency		Carbopol 974		ory drug (NSAID)	
17	Fluconazole	To compare vegetable oil versus liquid paraffin-based emulgel for fluconazole	Sesame oil	Carbo Pol 940	Oil in water emulgel	Fungal infections	Nailwal et al., 2019. (34)
18	Ornidazole	To formulate and evaluate a stable topical emulgel of ornidazole using different oils and gelling agents for enhanced drug release and retention	Clove oil, Mentha oil, Liquid paraffin	Carbopol 934, HPMC K100, Sodium alginate	Oil-in-water emulsion gel (emulgel)	Topical antimicrobial/antiprotozoal delivery	Raju, K. et al.,2019. (54)
19	Nimesulide	To prepare and evaluate sustained-release topical emulgel formulations of Nimesulid	Olive oil, Coconut oil	Carbopol 934, HPMC K15M	Oil-in-water (O/W)	NSAID / Anti-inflammatory	Ali & Ali, 2019. (69)

		e using conventional emulsions and assess the impact of formulation variables on drug release and physical properties					
20	Piroxicam	To formulate and evaluate piroxicam emulgel using Carbopol 934 and Xanthan gum for improved topical delivery	Oleic acid	Carbopol 934 (F1) and Xanthan gum (F2)	Oil-in-water (O/W) emulgel	Non-steroidal anti-inflammatory drug (NSAID)	Y. Bindu Vani et al.,2018. (62)
21	Lycopene (from tomato extract)	To develop a cost-effective extraction method for lycopene and formulate a stable topical emulgel with enhanced antioxidant delivery and thermal stability	Liquid paraffin	Carbopol 940	Oil-in-water (O/W)	Antioxidant / Anti-aging	Muhammad Sohail, et al., 2018. (67)
22	Terbinafine	To formulate and characterize a topical	Oleic acid	Carbopol 934	Nanoemulsion-based O/W emulgel	Antifungal / Dermatological	Paliwal, et al., 2018. (71)

		nanoemulgel of terbinafine to enhance skin penetration, stability, and bioavailability while avoiding first-pass metabolism					
23	Terminalia arjuna bark extract	To design and develop a novel emulgel formulation of T. arjuna bark extract for transdermal delivery, targeting controlled release and stability.	Olive oil	Carbopol 934 (0.5%)	Oil-in-water emulgel	Topical/transdermal drug delivery system for chronic ailments (e.g., pulmonary hypertension)	Gaikwad DT, Jadhav NR. Phcog Mag 2018. (72)
24	Lornoxicam	To formulate and evaluate a topical emulgel of Lornoxicam for systemic anti-inflammatory effect, minimizing GI side effects and dosing frequency	Light liquid paraffin	Carbopol 934, Carbopol 940, HPMC	Oil-in-water emulsion gel (emulgel)	Topical NSAID delivery	Mahaparale, S.P. & Gaware, V.,2017. (27)
25	Tioconazole	To develop, characterize, and	Light liquid paraffin,	Carbopol 934 and	Oil-in-water (O/W) emulgel	Antifungal agent (Imidazole class)	Shailendra Kumar et al., 2017. (58)

		evaluate tioconazole-loaded emulgel as an effective topical delivery system for hydrophobic drugs	Isopropyl myristate, Cetostearyl alcohol	Xanthan gum			
26	Capsaicin	To formulate and evaluate capsaicin emulgel for topical delivery to enhance solubility and therapeutic efficacy of the hydrophobic drug	Liquid paraffin (main oil phase), Clove oil (penetration enhancer)	Carbopol 974, Carbopol 930, HPMC K100M, HPMC K15M, HEC	Oil-in-water (O/W) emulgel	Analgesic / Topical anti-inflammatory	Navaneetha, K., et al., (2017). (64)
27	Tapentadol	To enhance solubility and permeability of Tapentadol via microemulsion-based emulgel for topical delivery, improving bioavailability and sustained release	Light liquid paraffin	Carbopol 981, Carbopol 934, Carbopol 940	Microemulsion-based O/W emulgel	Analgesic / Opioid	Ambhore, et al., 2017. (70)
28	Adapalene	To reduce systemic side effects and enhance	Soyabean oil	Carbopol 934	Nanoemulgel	Anti-acne agent (topical retinoid)	Khushboo et al., 2015. (55)

		topical efficacy of adapalene using nanoemulgel formulation with lower drug doses.					
29	Cyclosporin A	To develop and evaluate a polycarbophil-based emulgel for ocular delivery of Cyclosporin A with improved retention time and bioavailability	Castor oil	Polycarbophil	Oil-in-water (O/W) emulgel	Immunosuppressant for ophthalmic use	Yan Shen et al., 2015. (60)
30	Benzyl Benzoate	To formulate benzyl benzoate emulgel and evaluate its drug release efficiency compared to other topical formulations	Light liquid paraffin	Carbopol 934	Oil-in-water (O/W) emulgel	Acaricide, scabicide, pediculicide	Khuriah Abdul Hamid et al.,2015. (61)
31	Loratadine	To formulate and compare loratadine emulgels using different surfactants	Light liquid paraffin	Carbopol 940	Oil in water emulgel	Skin allergy, urticaria	Mahanat et al., 2014. (37)

32	Clotrimazole	To develop optimized clotrimazole emulgel and assess drug release and antifungal activity	Light liquid parrafin	Corbopol 934 And HPMC 2910	Oil in water emulgel	Fungal skin infection (Candida albicans)	Yassin, 2014. (40)
33	Metronidazole	To develop and optimize microemulsion based emulgel system for poorly water-soluble metronidazole using factorial design for enhanced drug release and spreadability.	Capmul 908 P	Xanthan gum	Microemulsion based emulgel	Topical Treatment for Infection	Rao et al., 2013. (32)
34	Insulin	To formulate and evaluate a transdermal insulin emulgel and assess its hypoglycemic effect in vivo	Emu Oil	Carbomer or HPMC (varied by formulation)	Transdermal Emulgel	Topical peptide delivery system	Muhammad Akram, et al., 2013. (73)
35	Spironolactone	Formulate spironolactone Emulgel for Topical Anti Androgenic Therapy	Light liquid paraffin	Carbopol 947P	Emulgel	Alopecia (Antiandrogenic)	Kapadiya et al., 2012. (53)

36	Mefenamic acid	Develop mefenamic acid emulgel and compare with diclofenac gel	Light liquid paraffin	Carbopol 940	Emulgel	Anti-inflammatory and analgesic	Khullar et al., 2012. (10)
37	Clotrimazole	To formulate and evaluate clotrimazole emulgel using carbopol 934 and methyl cellulose, and assess the effects of emulsifier concentration, oil phase type and concentration on drug release and rheology	Liquid paraffin and cetyl alcohol	Carbopol 934 and Methyl cellulose	Oil-in-water (O/W) emulgel	Antifungal agent	Yehia I. Khalil et al., 2011. (57)
38	Fluconazole	To evaluate Fluconazole topical delivery system for skin retention and antifungal use	Castor oil	Carboxy methyl cellulose	Micro emulsion based emulgel	Cutaneous mycosis, leishmaniasis	Salerno et al., 2010. (39)
39	Chlorphenesin	To optimize CHL emulgel using factorial design and	Light liquid paraffin	Carbopol 934 And HPMC	Oil in water emulgel	Fungal and bacterial skin infection	Mohamed et al., 2004. (38)

		evaluate drug release and antifungal activity					

XIV. Conclusion:

The detailed overview of Emulgel-based formulations from 2004 to 2025 emphasizes the amazing progress and versatility of this delivery technique in pharmaceuticals and cosmetics applications. Emulgels have emerged as a powerful platform for topical and transdermal drug delivery, offering a unique combination of gel and emulsion properties that enable enhanced drug solubility, controlled release, improved skin penetration, and patient-friendly application.

A wide range of active pharmaceutical ingredients (APIs) have been effectively added to emulgel systems in the thirty-nine studies that were examined. These include herbal and antioxidant agents like apple extract, lycopene, and propolis; antifungals like fluconazole and clotrimazole; and NSAIDs like celecoxib, meloxicam, and diclofenac. Oil-in-water emulgels are widely used because of their excellent spreadability, washability, and compatibility with both lipophilic and hydrophilic medications. Variants of nanoemulgel and microemulgel also show promise for improved bioavailability and targeted distribution, particularly in rheumatic and dermatological disorders.

The use of various oils (such as light liquid paraffin, oleic acid, castor oil, and essential oils), gelling agents (such as carbopol variants, HPMC, and xanthan gum), and emulsifiers designed to maximize stability, viscosity, and drug release kinetics has led to an evolution in formulation techniques. Recent research has emphasized the importance of precision formulation and repeatability through the use of factorial designs, QbD methods, and rheological modeling.

In summary, emulgels have developed into a reliable and flexible drug delivery system that can handle formulation issues for both natural and synthetic substances. Their use includes immunomodulatory, antiviral, antimicrobial, antifungal, anti-inflammatory, and cosmetic therapeutic areas. Emulgels are expected to become more and more important in topical and transdermal treatments in the future due to ongoing advancements in excipient selection, integration of nanotechnology, and patient-centered design.

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