Advances in Bioresearch
Adv. Biores., Vol 15 (5) September 2024: 401-407

Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.15.5.401407

Advances in Bioresearch

REVIEW ARTICLE

A Comprehensive Review on Emulgel as a Versatile Carrier System for Topical Drug Delivery

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ABSTRACT
Emulgel are novel drug delivery system which is a combination of gel and emulsion systems. Emulgel offers several benefits like nongreasy, easily removable, but a noteworthy is their capacity to add hydrophobic medications to gel bases that dissolve in water, a valuable trait since most of the drugs possess hydrophobic characteristics that hinder water solubility. This review delves into the key aspects of emulgel technology, including their formulation strategies, mechanisms of drug release and assessment parameters. By assessing the current state of emulgel research and development this review attempts to offer insightful information about the possibilities and difficulties of this new topical medication delivery technology, ultimately contributing to the advancement of pharmaceutical and cosmetic sciences.
Keywords: *emulsion, gel, emulgel, transdermal, hydrophobic*

Received 29.05.2024 Revised 25.07.2024 Accepted 30.08.2024

How to cite this article:
Priyanka K, Mukesh M. A Comprehensive Review on Emulgel as A Versatile Carrier System For Topical Drug Delivery. Adv. Biores., Vol 15 (5) September 2024: 401-407.

INTRODUCTION

In the realm of pharmaceuticals and dermatological treatments, the quest for an optimal method for delivering drugs m has led to significant advancements in the formulation of topical products [1]. Emulgel, a unique combination of emulsions and gels have become a viable option for improving the delivery of active pharmaceutical ingredients which are hydrophobic in nature to the skin [2]. This review aims to explore the evolving landscape of emulgel, shedding light on their formulation strategies, evaluation parameters for emulgel, advantages and disadvantages. Emulgel represent a versatile class of semisolid pharmaceutical formulations, engineered to combine the benefits of both emulsions (o/w or w/o systems) and gels. So, they offer an innovative means of delivering therapeutic agents, and treating various diseases like psoriasis, acne. The formulation of emulgel involves a delicate balance of surfactants, emulsifying agents, gelling agents, and active ingredients, all carefully chosen to achieve the desired texture, stability, and drug release profile.

Emulsion + Gel= Emulgel

Mechanism:

1.Drug Release:

Once applied to the skin, the emulgel adheres to the surface and begins to slowly release the drug.

The release of the drug occurs through a combination of diffusion and partitioning mechanisms. The drug can diffuse through the aqueous phase, oil phase, and the gel network to reach the skin.

The controlled release properties of the gel matrix and the formulation's composition determine the rate at which the drug is delivered over time.

2.Penetration:

The drug molecules, now released from the emulgel, penetrate the stratum corneum and enter the epidermis and dermis layers of the skin. This is the rate limiting step [3]. The emulgel unique composition helps in overcoming the skin's natural barrier properties, ensuring efficient drug delivery.

3.Systemic absorption:
Once in the skin's deepest layers, the drug can enter the systemic circulation, achieving the desired therapeutic effect.

Rationale of emulgel:

The traditional topical agents like creams, ointments and lotions are widely used but these topical agents have many disadvantages like grassiness, lesser spreading coefficient. To overcome this disadvantage these systems are incorporated into the gel base. Gel is composed of the 99% weight liquid and gelatin substances which form the macromolecular network of fibers and immobilize the water [4].
The dispersed phase act as reservoir which carries the active gradients [5,6]
Furthermore, emulgel exhibit enhanced bioavailability, making them a preferred choice for delivering hydrophobic drugs [2]. In the cosmetic industry, emulgel find extensive use due to their elegant texture, non-greasy feel, and ability to encapsulate active ingredients for controlled release. The rationale for emulgel lies in their ability to address formulation challenges, optimize drug delivery, and meet the diverse requirements of pharmaceutical and cosmetic applications.

Advantages:

Among the main benefits of emulgel are:
1.Enhanced Drug Delivery: Emulgel combine the properties of both gel and emulgel, permitting the efficient delivery of a wide range of pharmaceutical and cosmetic active ingredients. This dual nature enables improved drug penetration and absorption through the skin, making them effective for topical drug delivery [7].
2.Non-Greasy Texture: Emulgel have a pleasant, non-greasy texture that is well-tolerated by users. Unlike traditional creams and ointments, which can leave a heavy, greasy residue on the skin, emulgel provide a smoother and more cosmetically acceptable application [8].
3. Controlled Drug Release: Drugs can be released from emulgel in a regulated and prolonged way. By ensuring that the medication stays active for a longer amount of time, this controlled release profile lowers the need for frequent application and increases patient compliance [9].
4. Improved Stability: Emulgel have a stable formulation that helps protect sensitive pharmaceutical or cosmetic ingredients from degradation.
5. Versatility: Emulgel can be customized to suit various therapeutic and cosmetic applications. They can incorporate a large variety of active components, such as anti-inflammatory agents, antimicrobial.
6. Ease of Application: Emulgel are easy to apply and spread evenly over the skin. Their texture allows for smooth and uniform distribution of the active ingredients, ensuring consistent coverage and effectiveness [9].
7. Targeted Delivery: Emulgel can be designed to target specific skin layers or conditions. For instance, they can be formulated to release active ingredients at the epidermal or dermal level, depending on the therapeutic goals [10]
8. Transparent and pleasing appearance [9].

Disadvantages of emulgel:

1.Emulgel may cause skin irritation or allergic reaction in some individuals [11].
2.Some drugs are poorly permeable through the skin.
3. Bubbles are occurred during formulation of emulgel [11].

Types of emulgel:

Based on the droplet size and their distribution there are three types of emulgel [12].
1.Macroemulsion gel
2.Nanoemulgel
3.Microemulsion gel

1.Macroemulsion gel

The particle size of droplet is >400 nm.
This is opaque in nature.
Easily observed under an optical microscope.
Macroemulgels exhibit thermodynamic instability and can be rendered stable through the incorporation of appropriate surfactants [13].

2.Nanoemulgel.

The particle size of droplet is between 100-400 nm [14].
Nanoemulgel is transparent.
As the particle size of droplet is small, the Nanoemulsions have greater surface area. So greater the surface area greater the absorption.

3.Microemulgel

The particle size of droplet is between 10-100nm and usually made in association with cosurfactants [15,16,17].

Microemulsion gels are transparent.

This is thermodynamically stable.

Phase separation is not observed over wide temperature range.

Formulation of emulgel:

Emulgel ought to be non-comedogenic, non-toxic, and non-irritating.These properties of emulgel depend on the composition of emulgel. So, selecting the appropriate emulsifier, gelling agent, and oil phase are required [18].

Here is a basic formulation process for an emulgel:

Emulgel components:

Aqueous Phase:

The water and the alcohol are frequently employed. They are used for swelling of the gelling agent and aqueous phase in emulsion [19,20]

Oils (Lipophilic Phase):

The oil phase serves a dual role by acting as a vehicle for hydrophobic medications and shaping the ultimate product's physical characteristics, including its occlusive and sensory attributes. It plays a pivotal role in determining the emulsion's viscosity, permeability, stability, and drug release kinetics. For oral preparation most commonly, used oil are castor oil, maize oil, cottonseed oil [21,22].

Emulsifier:

During the emulsion preparation process, emulsifiers are utilized to aid in emulsification. Emulsifier ensure the physical stability during storage. Emulsifier decreases the interfacial tension between two phases. The emulsifier which is to be used is depend on their emulsification effectiveness, toxicity considerations, and the intended method of administration. The proper selection of emulsifier and its concentration is very important because it influence physicochemical properties of emulgel. While selecting the emulsifier HLB value plays important role. For water phase tween is used and for oil phase span is used. Common emulsifiers include nonionic surfactants like polysorbates (e.g., Tween 80) or cationic surfactants like stramonium bromide.

Gelling agents:

Gelling agents are added to create the gel structure. This are commonly employed to raise the viscosity of a preparation [27,28]. Gelling agent effects on the spreading coefficient, formulation viscosity, drug release profile, and system stability.

Preservatives:

These are included to prevent microbial growth and ensure the product's stability over time. While the ideal preservative would ideally work efficiently at low concentrations against a variety of microorganisms, Parabens primarily excel in their antifungal activity, and their antibacterial performance is less pronounced, especially against Gram-negative bacteria [35].

Phenoxyethanol is a preservative known for its broad-spectrum antimicrobial effectiveness, successfully combating the growth of Gram-negative and Gram-positive bacteria and yeasts [36].

Penetration enhancer (Optional):

These are added to improve skin permeability and enhance drug absorption. These agents aid in drug absorption through a range of mechanisms, including the temporary disruption of the skin barrier, changing the drug's distribution within skin components, and increasing the fluidity of lipid channels between corneocytes. Penetration enhancer interact with skin and increase permeability temporarily or reversibly [42].

Active pharmaceutical ingredient (API): The drug or therapeutic compound intended for delivery through the skin.

Formulation Process:

To create an emulgel, first, an emulsion is made by separately preparing an aqueous and an oily phase, incorporating the drug into the phase where it's more soluble, and then mixing these phases. Next, a gelling agent is dispersed in the aqueous phase to form a gel. This gel is then combined with the emulsion, resulting in an emulgel with the desired consistency and texture, effectively marrying the benefits of both gels and emulsions for various applications.

Finally, the third and concluding phase involves the emulsion and gel are carefully mixed and homogenized components in ratio 1:1 and add glutaraldehyde during mixing [46]. This step ensures the seamless integration of the emulsion and gel, resulting in a uniform and stable emulgel formulation.

Evaluation parameters:

1.Physical examination

The created emulgel was examined visually to make sure the colour, phase seperation,consistency and homogenesity.

2.Determination of pH

Determining pH is crucial. Using the digital pH meter, pH was found. The initial pH meter was adjusted. After being cleaned with distil water, the electrode was immersed into the mixture. Take three readings of the information.

3.Viscosity measurement:

The viscosity measurement was conducted utilizing a Brookfield viscometer. The formulation under investigation was moved into a beaker and given time to reach equilibrium for a duration of 30 minutes to ensure uniform consistency. Subsequently, the viscometer spindle was engaged at 50 revolutions per minute (rpm) and maintained for a period of 10 minutes. During this interval, the viscosity value of the formulation was accurately recorded.

4.Spredablity:

The spredablity of the emulgel formulation was quantitatively evaluated using a standardized apparatus consisting of 2 glass slides of predetermined dimensions. The experimental protocol involved the application of a defined quantity of the emulgel onto the surface of one slide. Subsequently, this slide was covered with the second slide, creating a uniform layer of the emulgel between them.

This assembly was then mounted on a specialized stand designed to secure only the lower slide in place, utilizing the mechanical grip of clamps equipped with opposing fangs. To initiate the spreading action, a mass of 20 grams was precisely positioned on the upper slide.

The critical parameter measured was the time required for the upper slide to completely disengage from the lower slide under the influence of the applied weight. This temporal metric serves as an indirect measure of the emulgel spredablity, with reduced detachment times indicating superior spreading properties.

5.Globule size and its distribution:

The determination of particle size and distribution was conducted using a Malvern Zetasizer instrument. Initially, Purified water was used to dissolve one gramme of the material and thoroughly mixed to ensure homogeneity. The resulting solution was then introduced into the photocell of the Zetasizer for analysis, yielding mean particle size and distribution data.

Alternatively, another method employed for assessing particle size and distribution involved the utilization of a Motic microscope. In this approach, the emulgel sample was placed onto a glass slide and subjected to microscopic examination to observe and analyze the characteristics of the globule size and distribution.

6. In vitro drug release study:

The Franz diffusion cell device was used to assess the drug release from the emulgel formulation in vitro., which is comprised of two main compartments: the sections designated for donors and recipients. An egg membrane served as a semipermeable barrier between these compartments and was securely fastened to prevent leakage. The surface of the egg membrane in the donor compartment received a homogeneous application of 500 mg of the produced emulgel. A buffer solution with a pH of 5.8 was prepared and utilized within the study to simulate the physiological conditions relevant to the drug release process. Throughout the experiment, 1 ml aliquots were periodical taken out at designated time intervals from the receiver compartment, which was initially filled with the pH 5.8 buffer solution. These aliquots were subsequently analyzed for their drug content employing UV-visible spectrophotometry. The percentage of cumulative drug release over time was determined by comparing the measured drug concentrations to a pre-established standard calibration curve. This methodological approach allowed for the precise quantification of the drug's diffusion rate through the egg membrane from the emulgel, providing insight into the formulation's release kinetics under simulated physiological conditions [47].

8.Microbiological assay:

The ditch plate method was employed for the assessment of the bacteriostatic or fungistatic properties, particularly suited for semi-solid formulations. Sabouraud's agar plates, prepared in advance and subsequently dried, served as the medium for this evaluation. Three grammes of the gelled emulsion were added to an already-cut trench in the agar plate.

Recently established microbial colonies were then inoculated onto the agar surface, utilizing inoculating loops to streak from the vicinity of the ditch outward towards the periphery of the plate, maintaining a perpendicular orientation to the ditch.

9.Skin irritation test

A modified Draize test was used to assess the test substance's propensity for causing skin irritation. Initially, the rats' dorsum was depilated in 4 cm2 of specified locations. The Gellified Emulsion was then evenly added to each prepared site in an amount of 0.5 g. The animals were housed individually after application. Following a 24-hour exposure period, the Gellified Emulsion was carefully removed, and the application sites were cleansed with tap water to eliminate any residual test substance. Observations for dermal reactions were then conducted, with the severity of irritation classified on a scale: 0 indicating "no observable reaction" (no patch reaction), 1 for "slight patchy erythema", 2 denoting "moderate patchy erythema", and 3 representing "severe erythema".

10.Stability studies:

The prepared emulgel (5 gm) were packed in suitable container. The ICH guidelines are followed in conducting the stability studies for the optimized batch. The prepared emulgel were subjected at "5 °C, 25 °C/60% RH, 30 °C/65% RH, and 40 °C/75% RH" for a 3 month. At interval of 15 days the emulgel were checked for its evaluation parameters. A stability investigation was conducted by monitoring the pH variation of the gel at consistent time intervals [48].

11. Drug content

10 gm of prepared emulgel was taken and mix it with 20 ml of methanol. Place it into the 100 ml volumetric flask. Then sonicate this for 30mi. Take the absorbance at specific wavelength [49].

12.Extrudablity

The force necessary to extrude a 0.5 cm ribbon of emulgel within a 10-second timeframe from a lacquered aluminium collapsible tube was quantified. This assessment was performed iteratively to ensure accuracy, and the mean value of the required force, obtained from repeated measurements, was utilized for subsequent calculations.

Table 1. List Of Emulsifiers [12,23-26]

Sr.no.	Emulsifiers	Concentration(%w/w)
1.	Tween 80	1.0 0.30 or 0.50 and 0.45 or 0.75 9 (nonionic)
2.	Combination of Tween 80 and Span 80	1.0 and 1.5 2.0 and 3.0 (nonionic)
3.	Soybean protein isolate	7.0 amphiphilic 4.0

Table 2.List of Gelling Agents [29-34]

Sr.no.	Gelling agent	Concentration used (% w/w)	Type of gelling agent
1.	Carbopol 934	0.5-2.0	Synthetic
2.	Carbopol 940	0.75–2.0	Synthetic
3.	HPMC	4.0–6.0	Semi synthetic
4.	Guar gum	0.5	Natural
5.	Xanthan gum	0.75 and 1.0	Natural
6.	Combination of Carbopol 934 and 940	0.5–2.0 and 1.0–2.0	Synthetic

Table 3. List Of Preservative [37,41].

Sr.no.	Preservative	Concentration (% w/w)
1.	Phenoxyethanol	0.2
2.	Methyl paraben	0.03 0.05
3.	Combination of methyl paraben ad propyl paraben	0.03 and 0.01 0.03 and 0.05

Table 4 . List Of Penetration Enhancer [43-45].

Sr.no.	Penetration enhancer	Concentration (% w/w)
1.	Mentha oil	4.0 and 6.0
2.	Menthol	1.0, 5.0, and 9.0
3.	Oleic acid	7.7 and 7.8

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