Role of emulgel in topical drug delivery system

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Abstract:

Topical drug delivery is primarily used for localized treatment in dermatology, but modern techniques are now being explored to enhance its systemic effects as well. Traditionally, topical preparations serve roles such as antiseptics, antifungal agents, skin emollients, and protective agents. The effectiveness of these formulations depends on several factors, including the solubility of the drug, the duration of contact with the skin, its lipophilicity, and skin permeability. Gels represent a relatively new dosage form, created by trapping large volumes of aqueous or hydro-alcoholic fluids within a network of colloidal particles. These gel-based formulations typically offer quicker drug release than traditional topical products. However, a key drawback of gels is their limited ability to deliver hydrophobic drugs effectively. To address this, a combination of gels and emulsions, known as emulgels, has been developed. Emulgels merge the beneficial properties of both emulsions and gels. Emulsions themselves are aesthetically pleasing and can be easily rinsed off. Emulgels offer several advantages in dermatological applications, including being thixotropic, non-greasy, easy to spread and remove, emollient, non-staining, stable, biocompatible, transparent, and visually appealing. They are currently used for the topical delivery of drugs such as analgesics, anti-inflammatories, antifungals, and anti-acne agents, as well as in cosmetic products, with further potential still to be explored.

Key words: Emulgel, Topical Drug Delivery, Gel, Hydrophobic drug, Transdermal delivery, herbal formulation, emulsion, lotions.

INTRODUCTION

Topical medication delivery systems: One of the easiest ways to administer drugs is through the skin. In addition to being a generalised drug delivery system that may be applied topically through the skin, ophthalmalmic, rectal, and vaginal passages, the topical drug delivery system has been used for centuries to treat local skin conditions. Topical medication delivery is not the same as applying a drug-containing formulation directly to the skin to treat a cutaneous condition. When alternative medication delivery methods (such as oral, sublingual, rectal, or parenteral) are ineffective or when a local skin infection, such as a fungal infection, occurs, the topical drug delivery system is typically utilised. Direct access to the skin as a target organ for diagnostic and treatment is made possible by topical medication delivery[1].

Skin to treat cutaneous disorders by having a pharmacological effect on the skin's surface or inside of it. Drugs administered topically must possess qualities such as a high partition coefficient, sufficient solubility in water and oil, and a low molecular weight (600 Daltons). The primary drawbacks of topical dose forms are that hydrophilic medications penetrate the stratum corneum layer of the skin, while hydrophobic pharmaceuticals diffuse and dissolve after delivery. Emulgel is therefore the preferred solution for overcoming these limitations.

Topical Drug Delivery

Topical drug delivery offers several advantages, including bypassing first-pass metabolism, avoiding gastrointestinal disturbances, allowing targeted delivery to specific sites, enhancing patient compliance, enabling self-medication, and being suitable for drugs with a short half-life or narrow therapeutic index. Additionally, treatment can be easily discontinued when needed.

However, there are also drawbacks, such as the potential for skin irritation, allergic responses, and limited drug absorption due to poor skin permeability. Large drug molecules, in particular, may not penetrate the skin effectively. The skin itself is a thick, complex barrier, and any substance must pass through the stratum corneum and any material present on the skin's surface to reach its target.[43]

There are two main categories of topical drug delivery systems: externally applied topicals and internally applied topicals. Externally applied topicals are spread, sprayed, or otherwise administered on the skin to cover and treat affected areas. In contrast, internally applied topicals are used on mucous membranes—such as those in the mouth, vagina, or rectum—for localized treatment

.Penetrating the skin membrane is a complex process and poses significant analytical challenges.Several factors influence the effectiveness of topical drug delivery. These include physiological factors such a pn oos skin thickness, level of hydration, presence of inflammation, skin pH, lipid content, density of hair follicles and sweat glands, and blood circulation. Additionally, physicochemical properties of the drug also play a role, such as its partition coefficient, molecular weight, degree of ionization, and the characteristics of the delivery vehicle.When a drug comes into contact with intact skin, it first encounters cellular debris, microorganisms, sebum, and other surface materials. The drug then diffuses through various

pathways, including hair follicles, sebaceous glands, and sweat ducts, ultimately passing through the continuous layer of the stratum corneum.[44]

Classification of topical drug delivery systems[45]

1. Solid: Powders, Plasters Ointments,

2. Semi solid: Creams, Poultices, Gels, Pastes

3. Liquid: Liniment, Lotions, solution, tinctures, Emulsions, Suspensions, Paints
4. Miscellaneous: Transdermal drug delivery systems, Tapes and Gauzes, Rubbing alcohols, Liquid cleanser, and Topical aerosol.

Emulgel

Emulgel, which combines the benefits of gels and emulsions, serves as a regulated drug delivery method for medications applied topically. These are water-in-oil or oil-inwater emulsions that are gelled by combining them with a gelling agent.The resulting formulation is called Emulgel and is jellified in a gel base to increase the emulsion's stability and penetration into the stratum corneum. Class II medicines have high permeability and poor solubility among the four BCS medication classes. For medications that are hydrophobic or poorly soluble in water, emulsified gel has been shown to be a more stable and effective. Show in fig 1,2.

Advantages of emulgel

1. avoiding a drug's systemic side effects, such as its first-pass metabolism.
2. The systemic circulation is either avoided or reduced.
3. Boost patient acceptance and compliance.
4. Appropriate for self-administration.
5. Deliver the medication to the body's intended location.
6. The ability to quickly stop taking medication when necessary.
7. It is rapidly absorbed by the skin and exhibits both hydrophobic and hydrophilic properties.
8. They are easy to use on hairy skin because they don't leave any residue or greasiness after application.
9. Better drug stability and release.
10. Improved loading capacity.
11. Production potential and low preparation costs.
12. No need for intense sonication.
13. Emulgel can be used to extend the effects of medications with shorter half-lives.
14. As an alternative to the oral route.
15. Preventing GIT absorption.
16. Avoiding pH-related inactivation.

Disadvantages of emulgel

1. Potential for allergic reactions.
2. Inadequate skin permeability of any medication.
3. Large-particle drugs are difficult for the skin to absorb.
4. The bubble's appearance during the emulgel's development.
5. Contact dermatitis causes skin inflammation.[2]

Constituents required for emulgel formulation

Addition to lipids and surfactants, a gel-based nanoemulsion formulation for topical application includes special ingredients such gelling agents, penetration enhancers, preservatives, and antioxidants. The medicine eventually reaches the required therapeutic concentration thanks to these penetration enhancers, which weaken the skin's defences and facilitate systemic drug entry.

Aqueous phase

The most popular aqueous phase for emulgel formulation is distilled or ultra-purified water, which is in charge of transforming emulsion form into emulgel when a gelling agent is present. [3]

Oils and lipids

The most important factor in the formulation of nanoemulsions is the choice of oils and lipids, which also determines the choice of additional ingredients like cosurfactants and surfactants. The principal application for pharmaceutically approved long-,

medium-, and short-chain triglycerides is in the formulation of nanoemulsions [4,5]. Medium-chain triglycerides are more appealing than long-chain triglycerides for emulsification due to their greater solubilising potential, while the majority of recently approved active pharmaceutical ingredients have limits in terms of solubility and permeability [6,7]. Due to their superior solubility for numerous medications, including Paclitaxel, short-chain triglycerides, such as triacetin, tributyrin, tricaprin, etc., are typically chosen over long-chain triglycerides [8,9]. It is important to make sure that the oil phase is pure and devoid of undesirable substances like peroxides when choosing oil and other lipid components.[10]

Vegetable oils

These oils, which are present in fatty acid glycerides, are derived from plants. Numerous plant-derived oils, including castor oil, soybean oil, peanut oil, coconut oil, almond oil, and olive oil, are authorised for topical medication delivery via a variety of drug delivery systems [11,12]. Many of these oils, including soybean and sesame oil, are also utilised to make Emulgel [13,14]. Because of the low drug solubility, these oils are fixed in nature and generally less desirable in many nanolipoidal compositions. By decreasing the resistance to permeation, these vegetable oils have been found to improve medication penetration to the skin in topical nanoemulsion formulations [15,16].

Fatty acids and alcohols

Plant oils contain a wide range of fatty acids. The majority of fatty acids are carboxylic acids with a lengthy, unsaturated or saturated aliphatic chain. Fatty alcohols, also known as long-chain alcohols, are typically straight-chain primary alcohols with a high molecular weight that can range from as few as 4-6 carbons to as many as [2226] carbons found in natural fats and oils. Numerous oils from the fatty acid and alcohol categories, including oleic acid, undecylenic acid, cetyl alcohol, stearyl alcohol, and oleyl alcohol, have been approved by the US FDA for topical medication administration [11]. Without the use of any chemical permeation enhancer, the produced emulgel exhibits improved permeability [14].

Surfactants and co-surfactants

Surfactants are employed in the production of emulgel to stabilise the finished formulation and aid in the drug's solubility. For this function, the surfactants can be cationic, anionic, or nonionic, among other chemical types. These surfactants are referred to as emulsifiers due to their function in emulsification. Emulgel is best prepared using nonionic surfactants such as polyoxyethylene sorbitan fatty acid esters and sorbitan fatty acid esters. Tween 20, Tween 80, and span 80 are frequently utilised for the formulation in this category. When creating nanoemulsions, choosing the right emulsifiers is crucial because of certain toxicity considerations. An elevated level of surfactants may cause skin irritation, which in turn may result in discomfort.[27]

Permeation enhancers

To increase the rate of transport through the skin and associated layers, permeation or penetration enhancers are preferable [27]. One of the key elements of the topical drug delivery system is a penetration enhancer, which is best utilised in topical nanoemulsion or emulgel [22,25]. These permeation enhancers primarily work by interacting with the components of the skin to temporarily and reversibly improve the permeability of the skin. Additionally, it gives drugs an extra push to enter the skin [26].

Gelling agents

One of the important ingredients in emulgel is the gelling agent, which gives the mixture its texture. These agents are cross-linking. Some of the gelling chemicals utilised in the production of emulgel include carbopole, poloxamer, hydroxypropyl methylcellulose, and tragacanth.

Preservatives

These are the chemical agents that extend the formulation's shelf life and shield it from microbial attack. Preservatives such phenol, propylparaben, benzoic acid, benzoalkonium chloride, and methylparaben are frequently utilised for creating nanoemulsions [27].

Antioxidants

These are the chemical agents used to protect the various components from oxidation. Butylated hydroxyl toluene, Ascorbyl palmitate, and Butylated hydroxyl anisole are the most preferred antioxidants in topical nanolipoidal preparation [28].

Preparation of emulgel

Emulgel is formulated by combining an emulsion and a gel, which are prepared separately before being mixed. The emulsion is created by blending the aqueous and oil phases, each prepared individually. Meanwhile, the gel is formed using a suitable gelling agent. Once both the emulsion and gel are ready, they are combined with gentle stirring. Common oil phase ingredients include castor oil, clove oil, and liquid paraffin, while water and alcohol serve as the aqueous phase components.[29, 30] Show in fig 3,4.

Evaluation of emulgel

1. **Physical Examination:**
The color, uniformity, consistency, and phase separation are evaluated in this process.[32]

2. **Spreadability:**
Spreadability of the emulgel is assessed based on its "slip" and "drag" characteristics. To measure Spreadability, an apparatus with a wooden block featuring a pulley at one end is used. A ground glass plate is fixed onto the block, and 2 g of emulgel is placed on it. Another glass slide is placed over it, forming a sandwich-like setup. A 1 kg weight is then applied on top, and the Spreadability is evaluated.

3. **Determination of pH:**
The pH is measured using a digital pH meter. The meter is immersed in the emulgel, and the pH reading is recorded. This process is repeated three times for accuracy.

4. **Rheological study:**
In a rheological study, viscosity is measured at 25°C using a cone and plate viscometer[33].

5. **In vitro drug release study:**
The process is conducted using a Franz diffusion cell, which is used to evaluate drug release [34].

6. **Microbiological assay:**

The ditch plate technique is used in this method to evaluate bacteriostatic or fungistatic activity.

7. **Accelerated stability studies:**

The procedure follows ICH guidelines, with the stability test conducted in a hot air oven at 37 ± 2 ºC, 45 ± 2 ºC, and 60 ± 2 ºC for a duration of three months [35]

8. **Drug content:**

The drug content is determined by UV spectroscopic analysis. The equation used is,

Drug content = (Concentration × Dilution factor × Volume taken) × Conversion factor

9. **Globule size and distribution in emulgel:**

The determination is carried out using a Malvern Zetasizer. The emulgel is dissolved in water, agitated, and then placed into the apparatus to measure the value.

10. **Centrifugation study:**

This method assesses the stability of the emulgel and is conducted one week after preparation. The study is performed using a minicentrifuge at 3000 rpm for 30 minutes.

11. **Skin irritation test:**

This test is crucial as the formulation is intended for topical use. It is conducted on animal skin by applying the emulgel and then returning the animals to their cages. After 24 hours, the animals are examined, and the emulgel is removed from the application site and cleaned with tap water.

12. **Stability studies:**
The emulgel was packed in aluminum collapsible tubes, stored under extreme conditions, and assessed for stability.

Conclusion

Emulgel is a modern tool for topical delivery of hydrophobic drugs with advantages of emulsion and gel to improve patient acceptability. Emulgel helps in enhancing spread ability, adhesion, viscosity, and extrusion. It is used both pharmaceutical and cosmetical applications as well as it allow to incorporate herbal formulations

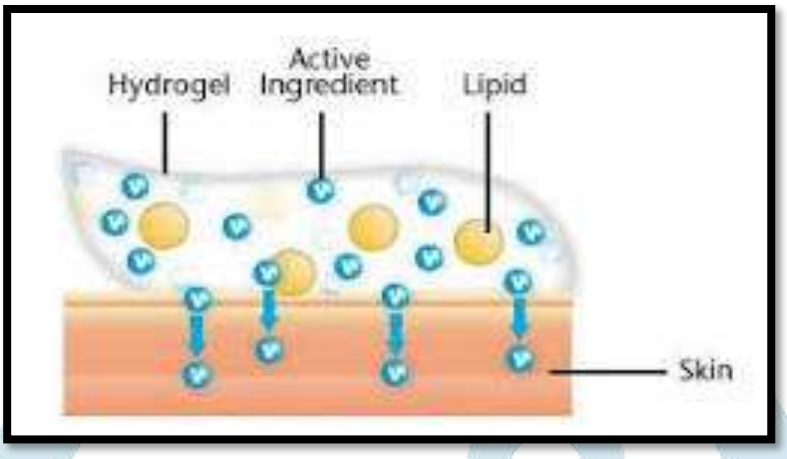

Fig. 1 Structure of emulgel

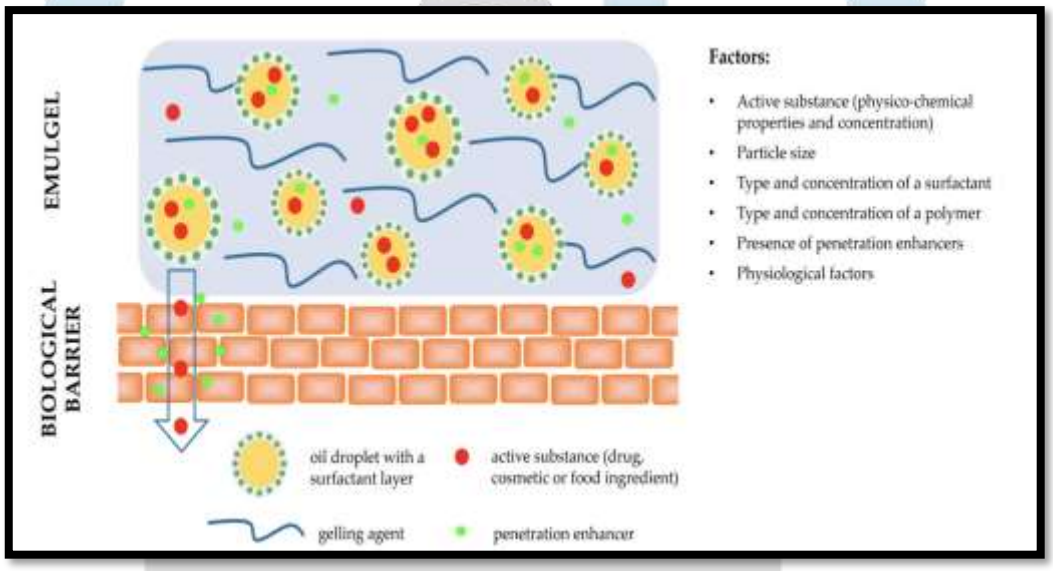

Fig 2 Mechanism of emulgel penetration through the skin

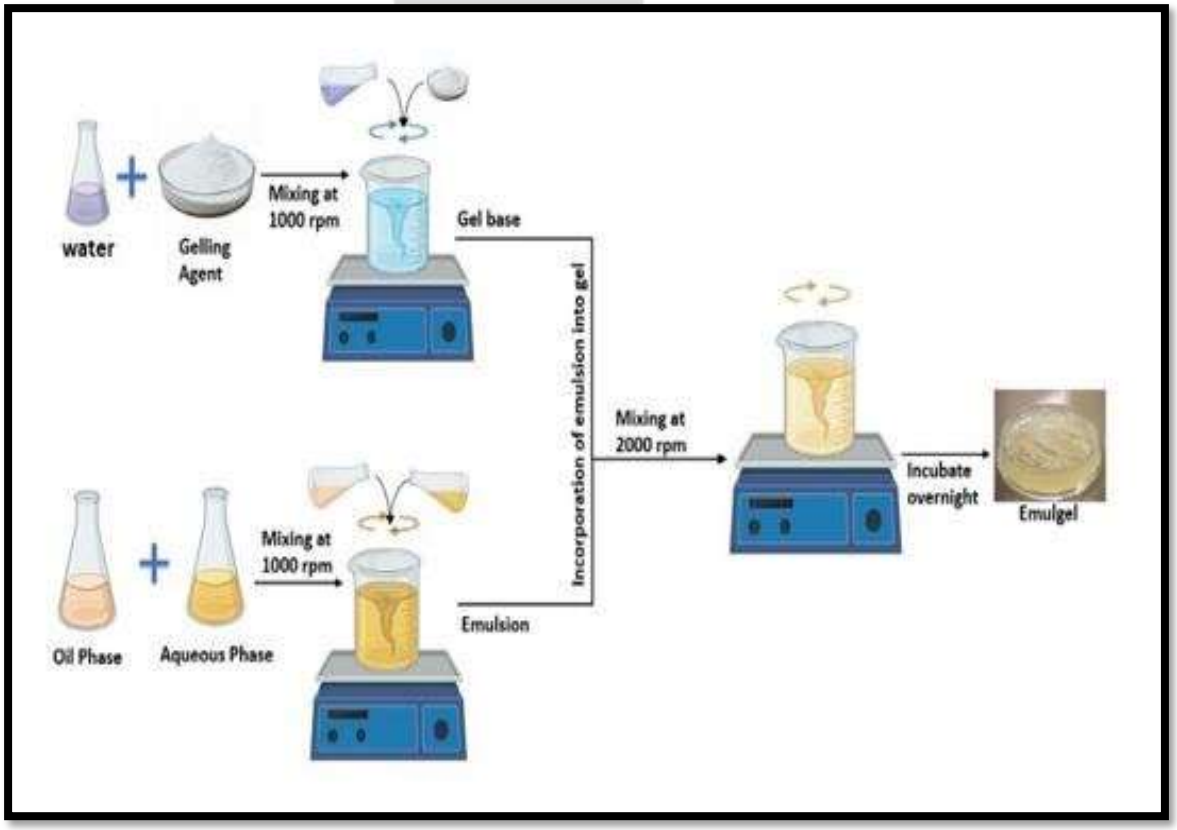

Fig 3 Preparation of emulgel

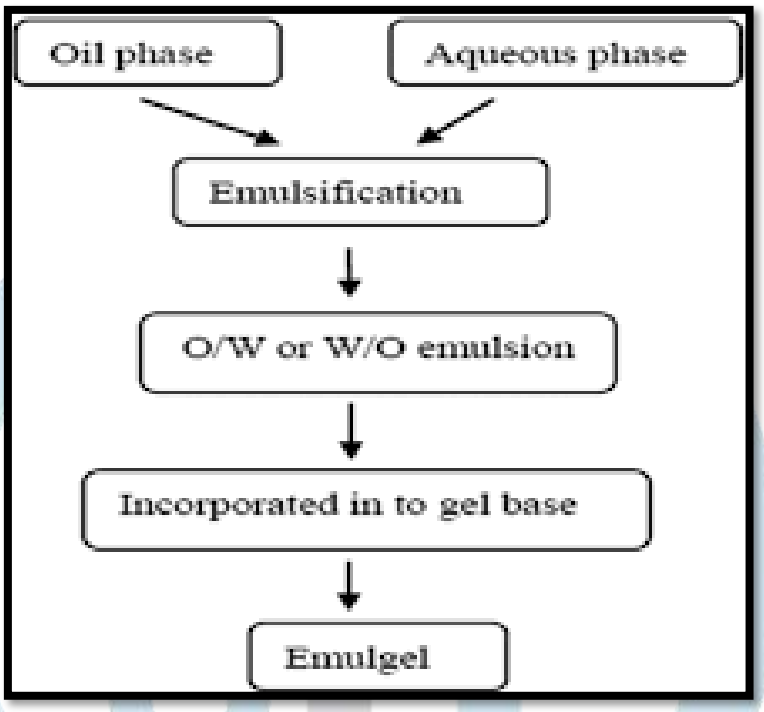

Fig. 4 Flow chart of emulgel preparation

Table 1 Current Elevations In Development Of Emulgel For Various Drugs

Drug	**Aim**	**Use**	**References**
Amphotericin B	Evaluation of the in vivo leishmanicidal activity of amphotericin B emulgel: An alternative for the treatment of skin leishmaniasis	Leishmaniasis therapy	36
Metronidazole and ciprofloxacin	Groundnut oil based emulsion gels for passive and iontophoretic delivery of therapeutics	Passive and iontophoretic delivery of therapeutics	37
Amlodipine besylate	Preparation of amlodipine besylate emulgels for transdermal administration and its percutaneous permeability in vitro	Transdermal delivery	38
Acyclovir and ketoconazole	Topical delivery of acyclovir and ketoconazole	Viral and fungal cutaneous manifestations	39
Lacidipine	Novel non-ionic surfactant proniosomes for transdermal delivery of lacidipine: optimization using 23 factorial design and in vivo evaluation in rabbits	Antihypertensive	40
Pravastatin	Optimised transdermal delivery of pravastatin		41
Ciprofloxacin	Genipin-Crosslinked Gelatin-Based Emulgels: an Insight into the Thermal, Mechanical, and Electrical Studies		42

Table 2 Marketed Emulgels

Sr No	Brand Name	Active Ingredient	Manufacturer	Use
1	Voltarol1.16% emulgel	Diclofenac Diethylammonium salt	Novartis	Anti-inflammatory
2	Diclon emulgel	Diclofenac diethylamine	medpharma	Anti-inflammatory
3	Diclomax Emulgel	Diclo fenac sodium	Torrent pharma	Anti-inflammatory
4	Miconaz-H-emulgel	Miconazole nitrate Hydrocortisone	Medical union Pharmaceuticals	Topical corticosteroid and antifungal
5	Dermafeet Emulgel	Urea 40%	Herbitas Intense	Moisturizing and exfoliation activity
6	Denacine emulgel	Clindamycin phosphate	Beitjala pharmaceutical company	Anti acne
7	Isofen emulgel	Ibuprofen	Beitjala pharmaceutical company	Anti-inflammatory
8	Diclona emulgel	Diclofenac diethylamine	Kuwait Saudi pharmaceutical industries co.	Anti-inflammatory
9	Dosanac emulsion gel	Diclofenac diethylammonium	Siam bheasach	Anti-inflammatory
10	Cataflam emulgel	Diclofenac potassium	Novartis	Anti-inflammatory

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