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Review on emulgel: A novel technique for drug targeting

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Abstract
This is a general review on emulgel as a drug deliver, which improves the drugs targeting and increases penetration through the skin, releases the drug in a controlled or sustained manner, and used for targeting of drugs to skin disorders. Emulgel drug delivery system can be considered as an emerging novel drug delivery system. These are biodegradable, relatively nontoxic, more stable and inexpensive. Emulgel has the potential to reduce the side effects of drugs and increase therapeutic effectiveness in various skin diseases. It can also be used as a carrier to deliver drugs topically. This review presents an overview of the types of emulgel, techniques of preparation of emulgel characterization and their applications.

Keywords: emulgel, novel drug delivery system, transdermal drug delivery system

Introduction
Human beings are affected by various diseases affecting their health and wellbeing. Efforts to treat these diseases have been accomplished by administering various drugs to the human body via various routes (topical, nasal, vaginal, oral, parenteral, etc.) [2, 5]. The route selection depends on the type and the severity of the disease [2]. Each drug delivery route has its advantages and disadvantages when compared to others. Skin is considered one of the heaviest single organs of the human body, consisting of about 10-15% of total body weight. It mainly consists of four layers; stratum corneum, viable epidermis, dermis, and subcutaneous tissue. The delivery through the skin is a topical drug delivery system [6]. Skin being the most readily accessible part of the human body, the molecules on surface application easily penetrate the skin via three routes: through intact stratum corneum (it presents about more than 99% of total skin area for percutaneous drug absorption), through sweat ducts, and sebaceous follicles [3]. Generally, topical drug delivery is used when the drug administration fails or in the local skin. Infection [1, 2]. Topical delivery is defined as directly applying a drug formulation to the skin to treat the cutaneous disorder [1, 4].

Drug delivery across the skin
The epidermis is the most superficial layer of the skin and is composed of stratified keratinized squamous epithelium, which varies in thickness in different body parts. Blood vessels are distributed profusely beneath the skin. The skin acts as a two-way barrier to prevent absorption or loss of water and electrolytes. There are three primary mechanisms of topical drug absorption: transcellular, intercellular, and follicular. Most drugs pass through the torturous path around corneocytes and the lipid bilayer to viable layers of the skin. The barrier resides in the outermost layer of the epidermis, the stratum corneum. Various penetration enhances and improves drug absorption through the stratum corneum to overcome this problem [6].

Emulgel
Emulgel is also called jellified emulsions. Emulsion in the gel has emerged as one of the most interesting topical drug delivery systems as it has a dual release system, i.e., emulsion and gel. Emulgel is either oil-in-water or water-in-oil type emulsions, which are gelled by mixing with a gelling agent [7]. Most pharmaceutical drugs are lipophilic compounds, which are practically insoluble in water. So to overcome this limitation, an emulsion-based approach is being used so that hydrophobic drugs can be easily administered to the skin. An emulsion may be defined as a dispersion of two or more mutually insoluble liquids, one in another [8]. The liquid is typically water and oil. A gel is a solid, jelly-like material formed

from a colloidal solution [9]. By weight, gels are mostly liquid, yet they behave like solids due to the addition of jelling agent. The presence of a gelling agent in the water phase covers a classical emulsion into an Emulgel. Emulsion possesses a certain degree of elegance. Gels for dermatological use have several favorable properties: thixotropic, greaseless, easily spreadable, easily removable, emollient, non-staining, longer shelf-life, water-soluble bio-friendly, transparent pleasing appearance [10]. Emulgel has high patient acceptability since it possesses the advantage of both gel and emulsion advantages. Therefore they have been recently used as vehicles to deliver various drugs to the skin. In recent years there has been great interest in the use of novel polymers with complex functions as emulsifiers and thickeners because the gelling capacity of these compounds allows the formulation of a stable emulsion and cream by decreasing surface and interfacial tension and at the same time increasing viscosity of the aqueous phase [11].

Gels

Gels are constituted by entrapment of large amounts of aqueous or hydroalcoholic liquid in a network of colloidal solid particles, inorganic or organic polymers of natural or synthetic origin. The higher aqueous component permits the more significant dissolution of drugs and permits easy drug migration compared to the ointment or cream base. However, this makes gels poor vehicles for hydrophobic drugs. This limitation of gels can be overcome by making emulgel[12].

Advantage and Disadvantage of Emulgel Formulation [12-13]

Advantage	Disadvantage
Hydrophobic drugs can be easily incorporated into gels.	Poor absorption of large particle size through the skin
It shows better stability.	Some drugs have poor permeability through the skin.
It has a better loading capacity.	Skin irritation or allergic reaction may occur
Production feasibility and low preparation cost.	During the formation of an emulgel, bubbles may occur.

Materials used in the formulation

Additives/Excipients used in Emulgel Formulation [14]

1) They must be non-toxic.
2) They must be commercially available in the applicable grade.
3) Their cost must be acceptably cheap.
4) They must not be contraindicated.

Aqueous Materials and oils

This forms the aqueous emulsion phase; commonly used agents are water and alcohol. Oil forms the oily phase of the emulsion. Mainly used oils in oral preparations are non-biodegradable mineral and castor oils and various fixed oils of vegetable origin. The examples of oil are given in Table no.1.

Table 1: Use of oils

S. No	Chemicals	Quantity
1	Isopropyl palmitate	7-7.5%
2	Isopropyl stearate	7-7.5%
3	Light liquid paraffin	7.5%
4	Isopropyl palmitate	7-7.5%

Emulsifiers

Emulsifying agents are used to promoting emulsification at the time of manufacture and to control stability during a shelf life for commercial preparations, e.g., Polyethylene glycol 40 stearate, Sorbitan mono-ole Polyoxyethylene sorbitan mono-oleate, Stearic acid, and Sodium stearate.

Gelling Agent

These are used to increase the consistency of any dosage form. They can also be used as thickening agents e.g., Carbopol 934P, Carbopol 940, Sodium carboxymethylcellulose, Hydroxypropyl methylcellulose. The examples of gelling agents are given in Table No. 2.

Table 2: Use of different gelling agents

S. No	Gelling agent	Quantity
1	Sodium C.M.C.	1%
2	Carbopol 934	1%
3	Carbopol 940	1%
4	HPMC 2910	2-2.5%
5	HPMC	3.5%

Permeation Enhancers:

These agents partition into and interact with skin constituents to induce a temporary and reversible increase in skin permeability. Some of these materials are given in Table No. 3.

Table 3: Use of different penetration enhancers

S. No	Penetration Enhancers	Quantity
1	Oleic acid	1%%
2	Lecithin	5%
3	Urea	10%
4	Isopropyl myristate	5%

Method of Preparation

Step 1: Formulation of Emulsion either O/W or W/O

Step 2: Formulation of gel base

Step 3: Incorporation of the emulsion into gel base with continuous stirring.

The gel in formulations is prepared by dispersing Carbopol-934 and Carbopol-940 in purified water with constant stirring at moderate speed. Then the pH of the gel is adjusted to 6-6.5 using triethanolamine. The oil phase of the emulsion is prepared by dissolving Span-20 in light liquid paraffin, while the aqueous phase is prepared by dissolving Tween-20 in purified water. Methyl and Propylparaben are dissolved in Propylene glycol while the drug is dissolved in ethanol, and both solutions are mixed with the aqueous phase. The oily and aqueous phases were separately heated to 70-80^{o}C; then, the oil phase was added to the aqueous phase with continuous stirring until cooled to room temperature. The gel and emulsion are mixed in a ratio of 1:1. Add glutaraldehyde during of mixing of gel and emulsion [15].

Characterization of Emulgel

Determination of pH

Topical formulations have a pH range between 5-6 measured using a pH meter. For pH determination, take 1g of product and dissolve in 10ml water pH of each formulation is done in triplicate to minimize error [16].

Globules size
To measure this parameter 1 gm of the product was dissolved in water and stirred to become dispersion, and then the sample was inserted into the photocell of Malvern Zetasizer [19].

Swelling Index
1 gm of prepared emulgel is taken on porous aluminum foil, and then dispersed in 10 ml of 0.1 N NaOH solutions. The sample removed on the various time intervals and weight is noted till no further change in weight:

Swelling Index (SW) % = [[Wt-Wo]/Wo]*100

Where
(SW) % = Percentage swelling,
Wo = Original weight of emulgel
Wt = Weight of swollen emulgel at time t

Bioadhesive strength
Accurately 1 gm of emulgel is applied between slides containing the rat's hairless skin pieces. Putting weight on a single glass slide creates some pressure to the removed sandwich of two slides. Adding extra weight is considered 200mg/min until the detachment of the skin surface. Required weight to detach the Emulgel from the skin will give bioadhesive strength. It is calculated by using the following formula:

$$Bioadhesive\ Strength = W / A$$

Where W= Weight required (in gms) and A=Area (cm2)

Determination of Rheological properties
20gm of prepared emulgel filled in 25ml beaker was used to measure viscosity by using Spindle number S64 by Brookfield viscometer [17].

Accelerated stability studies
As given in ICH guidelines, the formulations are kept in the oven at 37±2 °C, 45±2 °C, and 60±2 °C differently for three months. Drug content is examined every two weeks by an appropriate analytical method. Stability measurement is based on the change in pH of gel or degradation of the drug [18].

Drug content
1 g of prepared emulgel is mixed with 25 ml of methanol. This resultant solution is sonicated for 30 min. Drug content was analyzed using the suitable analytical method from this solution.

Spreadability
It can be determined by using the Slip and Drag method, as suggested by Mutimer; for this, take 2gm of emulgel and apply on lower side slide which is mounted with a wooden block and sandwiched is prepared by using other glass slide having the same size which is bind with a hook having 500mg weight placed. After 5 min additional weight was placed on the pan, which connected with the second slide. Time to cover 5cm distance for the upper slide was recorded and used to calculate spreadability by using the following formula:

$$Spreadability\ (S) = M * L / T$$

Where
M = Weight tied to upper slide,
L = Length of glass slides
T = time taken to cover the distance by upper slide

Skin irritation test
0.25 gm of prepared emulgel is applied to each different site (two to three sites/rabbit). When 24 Hrs of application, rabbit skin site are wiped and cleaned, Colour change of skin or undesirable change in morphology is recorded.

In-vitro Diffusion studies:
Franz diffusion cell is used to demonstrate diffusion study of prepared emulgel. A cellophane membrane is used during the study, and 0.5g of sample spread on membrane and diffusion is conducted for 8 Hrs at 37±1 °C using phosphate buffer (pH 7.4). At the 1 Hr. 1 ml sample is collected and replaced with a fresh buffer solution. Collected samples are analyzed by using a suitable analytical method [19].

Determination of Skin Permeation:
The chemical and structural changes in the epidermal layer are studied using differential scanning calorimetry (DSC). To assess the mechanism of permeation, thermal transitions in desiccated SC membranes of rats are investigated using the DSC technique. Both treated and untreated skin samples were previously hydrated on 27% Sodium-Br solution for at least 48 Hrs. to ensure lowering hydration to 20%. The skin samples are stored at silica gel for 3 days in desiccators prior to analysis. The skin layer is cut into pieces, and 4 mg weighted pieces are sealed in 10µL aluminum pans and placed in the differential scanning calorimetry unit and an empty pan as a reference. The flow of Nitrogen is adjusted to 20ml/ min, which serves as a purge gas. Samples are heated continuously at 10 °C/min rate for the range of 30-400 °C and fluctuation in DSC Graph is noted and studied [20].

Conclusion
Emulgel is a modern tool for topical delivery of skin disorders with the advantages of emulsion and gel to improve patient acceptability. Emulgel helps in enhancing spreadability, adhesion, viscosity, and extrusion. It is used in both pharmaceutical and cosmetic applications and incorporates herbal formulations.

Reference
1. Joshi B, Singh G, Rana AC, Saini S, Singla V. Emulgel: A Comprehensive Review on Recent Advances in Topical Drug Delivery, International Research Journal of Pharmacy. 2011;2(11):66-70.
2. Alexander AA, Khichariya A, Gupta S, Ravish Patel J, Tapan Kumar Giri, Dulal Krishna Tripathi. Recent Expansions in an Emergent Novel Drug Delivery Technology: Emulgel, Journal of Controlled Release. 2013;171:122-132.
3. Arpan Shah A, Kamal Kamdar, Rushabh Shah, Rajesh A, Keraliya, Emulgel. A Topical Preparation for Hydrophobic Drugs, Ph Tech Med, 2013 Oct;2:5.
4. Bhatt P, Gnanranjan G, Emulgels: A New Formulation Approach for Topical Delivery of Hydrophobic Drugs,

International Research Journal of Pharmacy, 2013, 4(2).
5. Singh P, Bala R, Seth N, Kalia S. Emulgel: A Novel Approach to Bioavailability Enhancement, International Journal of Recent Advances in Pharmaceutical Research. 2014 April;4(2):35-47.
6. Bhatt Preeti *et al*. Emulgels: A Novel Formulation Approach for Topical Delivery of Hydrophobic Drugs. International Research Journal of Pharmacy. 2013;4(2):12-15.
7. Gennaro AR. Ed. Remington, The Science and Practice of Pharmacy, 19th edition, Easton Mack Publishing Company, 1995, 285-299.
8. Kang L, Poh AL. Reversible Effects of Permeation Enhancers on Human Skin, European Journal of Pharmaceutics and Biopharmaceutics, 2007, 149-155.
9. Ashton P, Walter KA, Brain KR. surfactant effects in percutaneous Absorption: Effects on the transdermal flux of Methyl Nicotinate, International Journal of Pharmaceutics. 1992;87:261-264.
10. Elbayoumi TA, Torchilin VP. Liposomes for Targeted Delivery of Antithrombotic Drugs, Expert Opin. Drug Delivery, 2008, 1185-1198.
11. Mishra AN. Controlled and novel drug delivery, 4th Edn, CBS Publishers and distributors. 1997, 107-109.
12. Peneva P, Andonova V, Pilicheva B, Kassarova M. In vitrosurvey of Ketoprofen Release from Emulgels. Sci Tech. 2014;4:118-21.
13. Asija R, Sharma R, Gupta A. Emulgel: A Novel Approach to Topical Drug Delivery. Journal of Biomedical and Pharmaceutical Research. 2013;2(6):91-94.
14. Bhatt Preeti *et al*. Emulgels: A Novel Formulation Approach for Topical Delivery of Hydrophobic Drugs. International Research Journal of Pharmacy. 2013;4(2):12-15.
15. Baibhav J, *et al*. Development and Characterization of Clarithromycin Emulgel for Topical Delivery. International Journal of Drug Development and Research. 2012;4(3):310-323.
16. Modi J, Patel J. Nanoemulsion-Based Gel Formulation of Aceclofenac for Topical Delivery. International Jourmacy and Pharmaceutical Science Research. 2011;1(1):6-12.
17. Bonacucina G, Cespi M, Palmieri G. Characterization and Stability of Emulsion Gels Based on Acrylamide/Sodium Acryloyldimethyl Taurate Copolymer. American Association of Pharmaceutical Science Pharm Sci Tech. 2009;10(2):368-375.
18. Masmoudi H, Piccerelle P, Yveline Le D, Jacky kister A. Rheological Method to Evaluate the Physical Stability of Highly Viscous Pharmaceutical Oil-In-Water Emulsions. Pharmaceutical Research. 2006;23(8):1937-1947
19. Tanwar Y. A Jain Formulation and Evaluation of Topical Diclofenac Sodium Gel Using Different Gelling Agent. Asian Journal of Pharmaceutical Research and Health Care. 2012;4(1): 1-6.
20. Shakeel F, Baboota S, Ahuja A, Ali J, Shafiq S, *et al*. Skin Permeation Mechanism of Aceclofenac Using Novel Nanoemulsion Formulation. Pharmacies. 2008;63:580-584.