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Emulgel: A revolution in topical drug delivery system

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***Abstract*---**Topical delivery of drugs is one of the ideal routes of administrating a wide range of drug candidates and emulgels are emerging as a novel formulation, which exhibited the characteristics of both the emulsions and gels. Emulgel demonstrated improved penetrability during several studies and it is able to deliver hydrophilic as well as hydrophobic drugs and hence overcome the limitations of traditionally available topical preparations. More stable and effective emulgels can be prepared by nanonizing and micronizing the globules of emulsions, which improves the stability and half-life of Emulgels. The commercial availability along with the presence of strong clinical pipeline of emulgels is indicating towards the acceptance of this formulation while several advantages associated with this approach is also suggesting towards its potential as ideal topical drug delivery system. This article enlisted in-depth information about the emulgels, its components and structure along with the general method of production, evaluation and future scenario of this approach. The article also involved information about the patents insight, commercially available products and previously used drugs for developing stable emulgels.

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Keywords---emulgel, hydrophobic, microemulsion-gel, permeation enhancers, emulsifier.

Introduction

Skin is one of the largest sense organ of human body, which performs several essential functions and serves as first line barrier. It provides abbot 10% of the total body mass and have an average area of $1.7m^2$. (1) Skin also has ability to absorb the topically applied ingredients and hence the acceptance of skin as ideal route is increasing for delivering variety of drug molecules. (2) The structure of skin assists the topically applied ingredients to reach the various layers of skin as well as to reach the systemic circulation. Most of the ingredients penetrate the skin through three major pathways i.e. via stratum corneum, through sweat ducts and through the sebaceous follicle.(3) During the past few years, the topical drug delivery has emerged a novel approach, which is used for the management of several serious complications. The topical drug delivery system has some unique advantage due to which it is implemented when all the other routes of drug delivery are not able to exert the optimum therapeutic response. In addition to this, the topical route is also serving as ideal route for targeting the local skin infections such as fungal or bacterial skin infections.(4, 5)

The topical drug delivery approaches are mainly classified on the basis of their consistencies and includes solid preparations, liquid preparations, semi-solids and miscellaneous preparations. The selection of dosage form depends on the nature of the drug as well as the target site. Along with this, the penetrability of the drug also depends on some physiochemical factors including thickness of skin, pH, hydration, lipid content, blood flow, density of hair follicles, density of sweat glands, partition coefficients and molecular weight etc.(6-8)

Currently, the available topical drug administration technologies are able to deliver the hydrophilic drugs only and the inability to deliver the hydrophobic drugs is one of the major limitations for this approach. Emulgel is one of the recently developed formulations, which is able to deliver both the hydrophilic and hydrophobic drugs. It is closely related to the gels, which consist of a colloidal network that hold a large amount of water or hydroalcoholic solution. It provides improved solubility of drugs and hence improved the penetrability of the drug and consider as one of the ideal approach for topical delivery of drugs. Besides the benefits of the gels, it is also unable to deliver the lipophilic drugs and hence Emulgels are developed to overcome this limitation.(9, 10)

Emulgel is a combinational formulation consisting of emulsion and gel and the type of combination depends upon the nature of drug so that maximum bioavailability can be achieved.(11, 12) The benefits of Emulgel over the traditional topical administration including thixotropic, greaseless, improved spreadibility, easily removable, biodegradable, emollient and better convenience. Along with this, high stability and improved shelf life of Emulgel is also encouraging the researchers to develop new products belonging to this class.(13, 14)

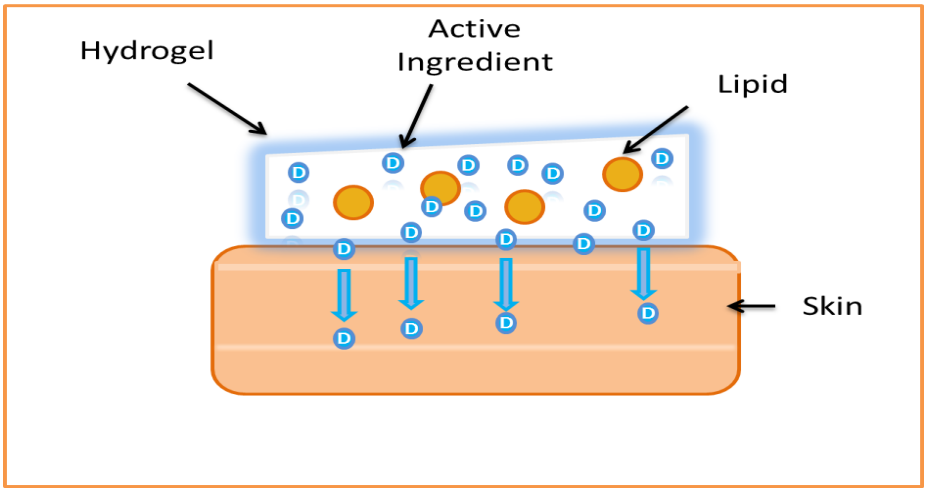

Figure 1: Structure of Emulgel

Structure of Skin

Skin is composed of three major parts i.e. epidermis, dermis and subcutaneous tissues. Epidermis is the outermost layer while dermis is located beneath the epidermis. Subcutaneous layer consist of fatty cells and tissues.(15)

Epidermis

It is the outer layer of the skin, which comes in the direct contact with the topically applied ingredients and it is non-vascular in nature. Epidermis performs the barrier function and forms a protective covering made up of stratified squamous epithelium cells. Epidermis is divided into 5 layers i.e. Stratum corneum, stratum lucidum, stratum granulosam, stratum spinosum, and stratum basale. Stratum corneum is the outer most layers, which is the thickest layer (20-30 cells) while the stratum basale is the innermost layer. (16, 17)

Dermis

It performs a major function of providing physical support to the epidermis and nourishes the cells of the epidermis. Dermis consist of two layers i.e. papillary layer and the reticular layer and both the layer consist of substances such as elastin, fibrillin and collagen. In addition to this, dermis also consists of some essential glands such as sebaceous glands, sweat glands along with hair follicles, blood vessels and nerve endings. Some smaller blood vessels are also present in this layer, which provides nourishment, elasticity and oxygen to the epidermis.(18, 19)

Subcutaneous layer

It consists of fatty cells and tissues, which provides a cushion like protection to the body and performs the function of insulation. (15)

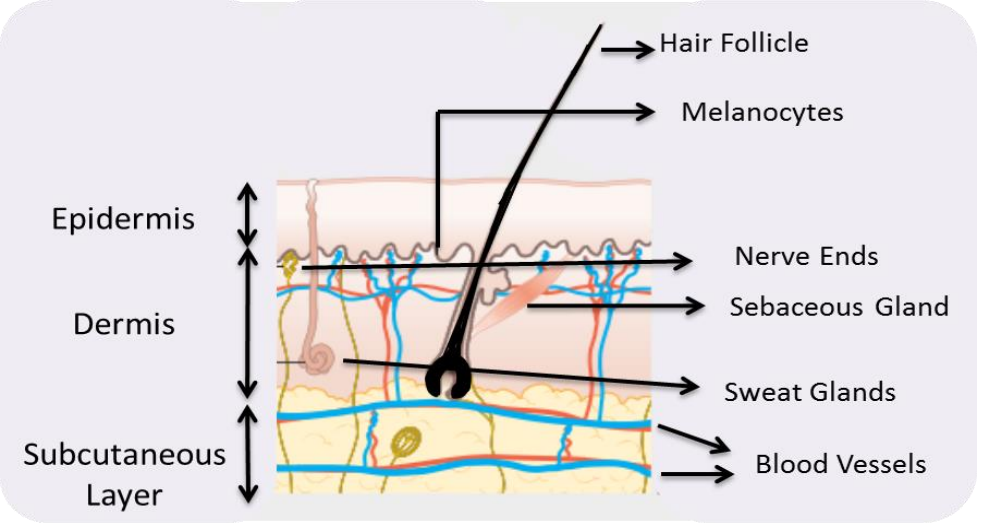

Figure 2: Structure of Skin

Penetrability of the Skin

For reaching the systemic circulation and to provide the local effects, the topically applied active ingredient should cross the various layers of skin and the major pathways for crossing the skin involved intercellular penetration, follicular penetration and transcellular penetration. Intercellular penetration involves the transport of drugs through the junction between the epithelial cells. (20) Transcellular penetration is defined as the transport of drug across the epithelial cells. (21) In the case of Follicular penetration, the drug passes along with the hair follicles to cross the skin barriers.(20)

Factor Affecting Penetrability & Absorption of Topically Applied Products (6, 7)

1) Skin Hydration
2) Vascularity
3) Lipid Content
4) pH of Skin
5) Density of Hair Follicles
6) Density of Sweat Glands
7) Inflammation of Skin
8) Lipid Contents
9) Partition Coefficients
10) Molecular Weight
11) Degree of Ionization
12) Type of Vehicles

Approaches for Improving the Penetration & Absorption Rate (22)

1) Chemical Enhancement
2) Physical Enhancement

3) Biochemical Enhancement
4) Supersaturation Enhancement

Emulgel - Advantages & Disadvantages

Advantages of Emulgel

1) The biggest advantage of emulgel is that it can easily deliver the lipophilic drugs by incorporating the drug with the gel based drug-oil-in-water emulsion. During the incorporation of lipophilic drugs directly in gel, solubility acts as the major challenge, which resists the release of drug into the systemic circulation. The Emulgel improves the stability and drug release profile of the lipophilic drug by combining the benefits of emulsion and gel in a single formulation. (23, 24)
2) As compared to the other topical formulations, Emulgels are the most stable formulation and demonstrated longer shelf life. In case of topical powders, hygroscopic nature is the major problem while phase inversion is leading problem in case of topically applied creams. There is no such problem in Emulgel and hence it is superior to other traditional topical preparation. (23)
3) Another important advantage of Emulgel is that it has greater loading capacity as compared to the alternative topical preparations. The loading capacity of emulgel is also higher than the novel niosomes and liposome based preparations as the entrapment efficacy is low in nanoparticle based topical preparations. (23)
4) Emulgels are cost efficient as the cost of production is comparatively less in the case of this this dosage form. The process of development is simple having few steps and no special instruments and equipment are required during the production. Most of the ingredients are easily available and cheaper, which reduce the final cost of the emulgel. (23, 25)
5) Emulgel are also able to provide controlled release of the active ingredients and hence improve the half-life of the drug. (26)
6) The production of Emulgel doesn't required intense sonication and hence probability of drug degradation and leakage is lesser. (26)
7) Emulgel also provides higher patient compliance as compared to the conventional products. (26)
8) It helps in bypassing the first pass metabolism and prevents the gastrointestinal adverse reactions. (27)
9) Helps in achieving targeted action and the therapy can be terminated easily when required.(27)

Figure 3: Advantages of Emulgel

Disadvantages of Emulgel

1) Drugs with higher molecular weight and particle size are unable to absorb the drug via skin.
2) Sometimes, formation of small bubbles may occur in Emulgel, which reduces the penetrability of drug.(28)
3) Skin Irritation is also very common.(29)

Classification of Emulgel

Emulgel can be classified in three major categories on the basis of particle size i.e. macroemulgel, nanoemulgel and microemulgel.

Macroemulgel

These are the most widely used emulgels having a particle size of more than 400nm. These emulgels are opaque and homogenous but the droplets of emulsion are easily detectable when observed under microscope due to large particle size, macroemulgels are thermodynamically unstable.(30, 31)

Nanoemulgel

This emulgel is prepared by incorporating nanoemulsion with the gel with an aim of developing thermodynamically stable dispersion, which is transparent and homogenous in nature. The size of droplets is less than 100nm in the case of nanoemulgel and hence better permeability can be achieved.(30-32)

Microemulgel

Microemulgels are the preparations with particle size in the range of 10 to 100nm and serve as a thermodynamically stable formulation. The composition of microemulgel is such that it assists the drug to cross the skin and reach the targeted site. In addition to this, microemulgels are able to overcome the limitations of both the microemulsions and gels. High viscosity, permeability and homogeneity of microemulgel are the major advantages of this system over various traditional topical therapies. (30, 31, 33)

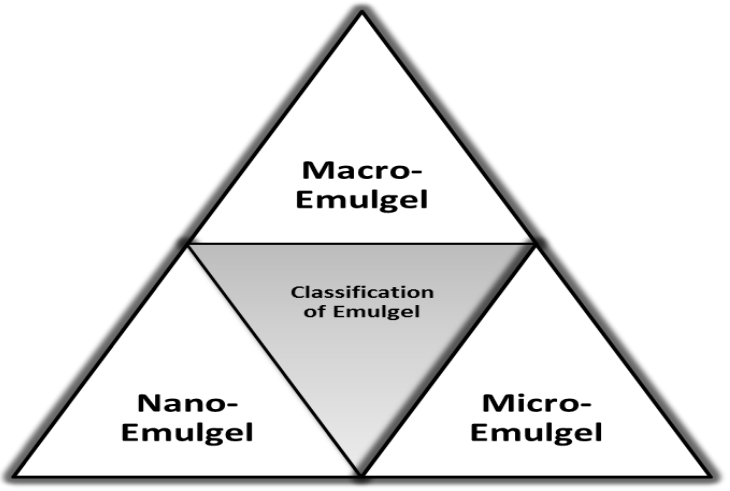

Figure 4: Globule Size Based Classification of Emulgel

Components of Emulgel

Emulgels mainly incorporates emulsions with the gel to develop ideal formulation for delivering the lipophilic as well as hydrophilic drugs. The emulsion used for the preparation of Emulgel may be oil in water or water in oil, depending on the nature of drug and hence helps in improving the bioavailability of the drug by formulation ideal formulation. The essential components of the Emulgel involve aqueous material, oils, emulsifiers, gelling agent and permeation enhancer. (34)

Aqueous Material

Water and alcohol are the most commonly used aqueous material, which forms the aqueous phase of the emulsion. (34)

Oils

Oils are used for the development of oily phase of the emulsion and mineral oils are the most commonly used oils for the development of emulgels. The mineral oil can be used alone or in combination with other oils, especially along with hard and soft paraffin. Further, castor oil can also be used due to its laxative properties. Some other oils used due to their medicinal properties are Onesuch oil, jojoba oil, archais oil, cottonseed, maize oil, fish liver oil etc. (26, 35, 36)

Emulsifiers

The most essential component for maintaining the stability of emulsion is emulsifier, which are generally surfactants used for the process of emulsification. For the formation of oil in water emulsion, the nonionic surfactants including spans, tweens with HLB higher than 8 are used while the mineral oils such as liquid paraffin have HLB less than 8 and hence used for development of water in oil emulsion. Some of the most commonly used emulsifiers are PEG 40 stearate, Span 80, Tween 80, Stearic acid, sodium stearate etc. (26, 37-39)

Gelling Agent

These agents are used to provide gel like properties to the formulation to improve the consistency. Several studies demonstrated that the concentration of the gelling agent is inversely proportional to the extent of the drug release. The most commonly used gelling agent for the development of emulgel are Carbopol, HPMC 2910, HPMC K4M etc. (26, 40, 41)

Permeation Enhancer

These are the agents responsible for improving the penetration power of drug by implementing various mechanisms to improve the permeability of skin. One of the major mechanisms involves the disruption of stratum corneum or by altering the proteins of skin. Some of the most commonly used ingredients for enhancing the permeability are oleic acid, clove oil, lecithne, euclyptous oil, menthol etc. (42-45)

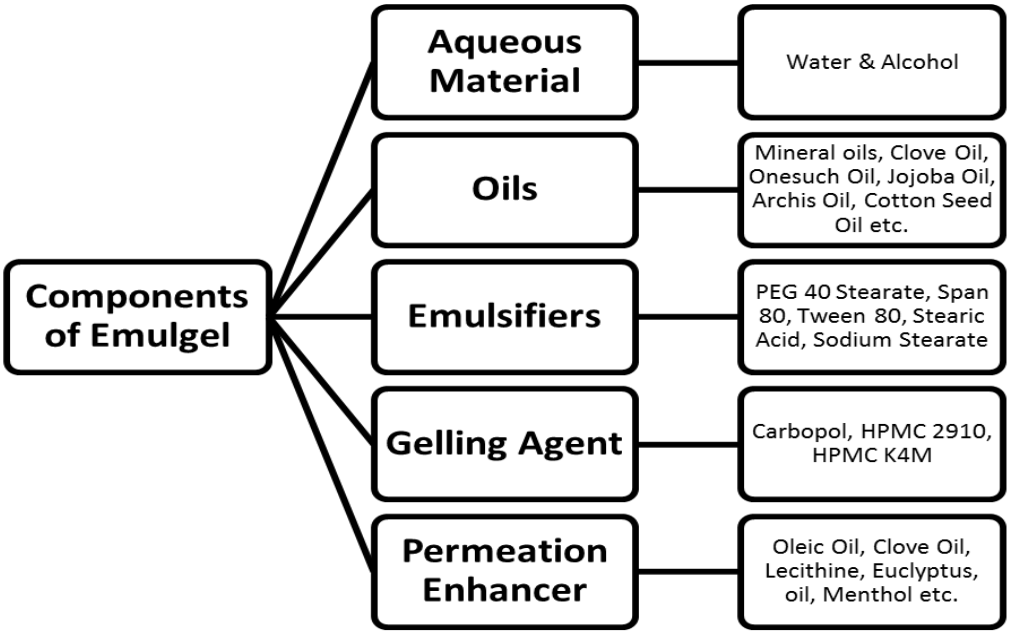

Figure 5: Components of Emulgel with Commonly Implemented Examples

Method of Preparing Emulgel

As the name indicates, emulgel consist of two major components i.e. emulsion and gel. Both these components are prepared separately and then incorporated to formulate Emulgel. First, emulsion is prepared by the mixing the aqueous and oily phase together to generate a homogeneous biphasic dosage form. After that, a normal gel is prepared by adding gelling agent. The gel and the emulsion are then mixed gently to develop emulgel. (44)

One more method used for the development of Emulgel involves three major steps i.e. dispersion of polymer in water, neutralization of the polymeric aqueous dispersion and emulsification of the oil phase. The polymer is dispersed by stirring at 900 rpm for 20 minutes and the prepared slurry is then neutralized by using sodium hydroxide solution, which makes the solution clear and stable gel. The polymer is then subjected to complete hydration of the gel.(27)

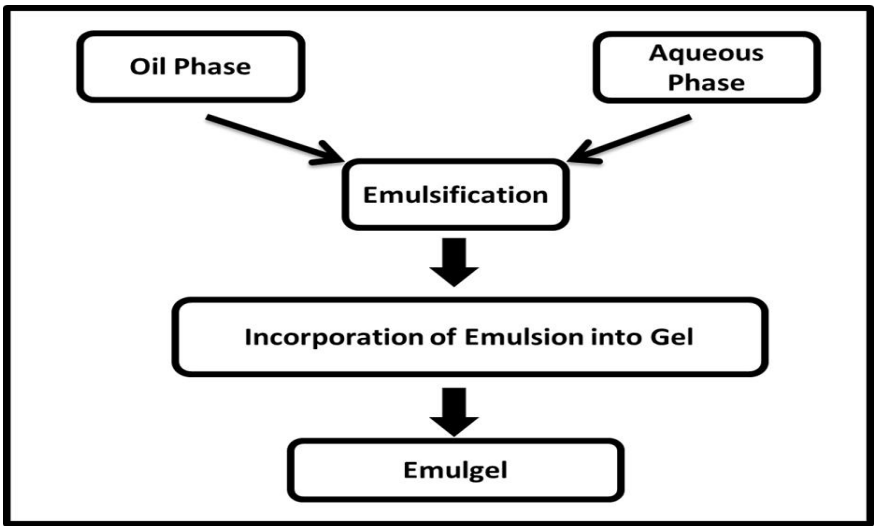

Figure 6: Emulgel – Method of Preparation

Evaluation of Emulgel

1) Physical Appearance: The prepared emulgel is evaluated for the physical appearance by considering color, consistency, homogeneity, grittiness, pH and phase inversion/separation. For measuring the pH, 1% solution of the emulgel is prepared and pH is observed accurately by using digital pH meter. (45)
2) Drug Content Measurement: For measuring the drug content, 1gram of emulgel is converted into a solution by mixing it with a suitable solvent in a sonicator. The prepared solvent is then filtered and absorbance is measured using UV spectrophotometer.(46, 47)

Drug Content = (Concentration x Dilution Factor x Volume Taken) x Conversion Factor

3) Rheological Studies: Viscosity is one of the major parameter for emulgel, which is measured by using Brookfield viscometer at a temperature of 25°C. For measuring the viscosity, the emulgel is introduced into the beaker and the spindle is allowed to rotate in the beaker freely and the reading was noted from the digital indicator.(44, 46)
4) Spreadability: Spreadability is a measure of slip and drug abilities of the emulgel, which is determined by calculating the spreading coefficient using apparatus suggested by the Multimer. The apparatus has a woodeb block, which is joined with a pulley while the ground glass slide was placed over the block. About 2gm of the emulgel is placed over the slide and it is subjected to sandwich between the fixed slide and the movable slide of the same dimension. A weight of 500gm is then placed over the sandwiched for duration of 5 minutes to form a uniform film of the emulgel over the slides. After that, a desired quantity of weight is placed and the taken by the slides to cover a distance of 5cm is noted to measure the Spreadability coefficient. (44, 48, 49)

$$S = M.L/T$$

Here, S = Spreadability
M = Weight Applied
L = length of glass slide
T = time taken to cover distance of 5cm

5) Extrudability Test: Extrudability is a parameter indicating towards the amount of pressure required to extrude the material from the tube containing emulgel. It is calculated by measuring the weight required to extrude 0.5cm ribbon of emulgel from aluminum tube in duration of 10 seconds. Generally, this test is performed for getting three readings and the average of all the measurements will be considered to calculated by using the following formula: (43, 50)

$$\text{Extrudibility} = \text{Weight Applied (gram)} / \text{Area (cm}^2\text{)}$$

6) Skin Irritation Test: This test is also known as patch test. For conducting this test, rats are used, which are shaved prior conducting the test and a specific amount of the emulgel is applied over the surface of dimension 2.54cm x 2.54cm. The application site is then observed for the presence of any adverse events such as redness, irritation, alteration in morphology, inflammation etc. The test is conducted on the 8 rats and the emulgel will fail the test if adverse event is observed in more than 2 rats. (51, 52)
7) Globule Size & Zeta Potential: Similar to the emulsions, the emulgels are also evaluated for measuring the zeta potential and size of the globules, which indicates towards the stability of the formulation. This test is performed by using Zetatrac, which measures the potential by considering the response of charged particles to electric field.(15, 53, 54)
8) Biodhessive Strength Measurement: This test is a measure of force of adhesion of the emulgel and it is measured by using an apparatus consisting of two arm balance. One arm consists of two glass plates containing the fresh skin of rat while the other arm consists of single glass plate. Both the arms are then balanced by adding some weight and kept it

for duration of 5 minutes. For performing the test, about 1gm of the emulgel is taken and placed between the two slides containing the rat skin so that both the slides attach to each other. After that, extra weight is applied on the other arm at a rate of 200gm per min until both the slides get detached. The weight at which the slides detached is considered as a parameter for adhesive strength and it is calculated by using the following formula: (47, 55)

$$\text{Biodhessive strength} = \text{weight required (in gram)} / \text{Area (cm}^2\text{)}$$

9) Stability Studies: For performing the stability studies, ICH guidelines are followed and accelerated studies are generally preferred. The emulgels are filled into the collapsible tubes and introduced to temp of 37 ±2°C, 45±2°C and 60±2°C and relative humidity of 60% to 75% for a period of 3 months. The samples are then subjected to analysis after every 15 days for parameters such as pH, physical appearance, rheology, drug content and drug release profiles. (51, 52)
10) In-vitro Drug Release Study: For conducting the in-vitro drug release profile of emulgel, diffusion cells are used, which involves the use of dialysis membrane. For conducting this test, the dialysis membrane is soaked in phosphate buffer pH 5.5 for duration of 9 to 12 hours. This membrane is placed at one end of the hollow tube of cell and the emulgel is applied uniformly over the membrane. The receptor compartment, which is adjacent to the donor compartment, is filled with the phosphate buffer pH5.5 and the temperature is maintained to 37°C while he solution is mixed continuously during the test. After that, 5ml of sample is withdrawn from the solution at regular interval, which is analyzed by using US spectrophotometer to estimate the amount of drug release. The percentage drug release is then calculated by using the value of absorbance and standard curve of the drug.(43, 56)
11) Swelling Index: The swelling index is also considered for evaluating the emulgel and it is measured by taking 1gram emulgel over the aluminum foil, which is placed in a 50ml beaker containing 10ml of 0.1N NaOH. The samples are then withdrawn from the beaker at regular interval and dried. The change in weight is considered as parameter of swelling index and it is calculated by following formula. (43, 46, 56)

$$\text{Swelling Index (SW)} \% = [(W_t - W_0)/W_0] \times 100$$

Here, W_t= Weight of Emulgel after time t
W_0= Weight of Emulgel after time zero

12) Ex-Vivo Permeation Studies: The ex-vivo permeation studies is conducted on the animal model by using healthy male rats. The rats are first prepared for the test by removing the hairs and the area is washed properly. This skin is then removed from the rat and attached to the donor compartment and the permeation study is then performed by applying the emulgel over the skin in the similar manner of in vivo studies. Phosphate buffer is filled in receiver compartment and sample are taken at regular interval to observe the absorbance using the UV spectrophotometer.(57)

13) Microbiological Assay: The microbial assay is performed to detect the presence of microorganism in the emulgel. For performing this test, Ditch plate method is most commonly used, which is able to detect the bacteriostatic and fungistatic activity of the semisolid formulations. The method of conducting this test involved the use of Sabouraud's agar dried plates and the emulgel is subjected to these plated at right angle to the edge of plate. The plates are incubated for 18 to 24 hours at 25°C and the fungal growth is observed. The % inhibition is then calculated by using the formula: (58)

$$\% \text{ Inhibition} = L2/L1 \times 100$$

Here, L1 = total length of the streak culture
L2= length of inhibition

14) Syneresis Measurement Test: In the case of emulgel, the shrinkage of the formulation is observed sometimes, which resulted in the release of liquid and this phenomenon is termed as Syneresis. For measuring this activity, the emulgel is introduced into the cylindrical tube, which has small pores at the bottom and covered with whatman filter paper. This system is then placed in centrifuge and operated for 15 minutes. The separated liquid is then weighed and % Syneresis is then calculated by using following formula:(59)

$$\% \text{ Syneresis} = (\text{Weight of Separated Liquid} / \text{ Total Weight Before Centrifugation}) \times 100$$

Future Scenario of Emulgel

Emulgels are one of the rapidly emerging formulations for the topical delivery of active constituents and the market acceptance of the available products of this class is indicating towards the future potential of this class. As a large number of currently available drugs are hydrophobic in nature, emulgel is expected to emerge as ideal topical formulation as most of the traditional approaches are unable to deliver the hydrophobic drug candidates. The application of emulgel results in better absorption and bioavailability of drugs. Besides numerous benefits of emulgels, some adverse events are also associated with this formulation in which bubble formulation is the major one. (60, 61) For overcoming these limitations, the researchers are focusing on the development of micro and nano emulgels, which are more stable and able to minimize the risk of bubble formation. (15, 62)

Recently, the introduction of nanotechnology in nanonizing and micronizing the particles of emulsion is initiating a new revolution in this segment, which results in the development of emulgels with enhanced drug penetrability and bioavailability. (15) Along with this, the researchers of leading pharmaceutical companies are also working to develop emulgels containing herbal oils with medicinal properties and this field has potential to open tons of opportunities in upcoming years.(63) Further, the other benefits of emulgels such as controlled

release application, rapid drug release, better drug loading capacity etc. are indicating towards development of more efficient and productive formulation and it is expected to appear as ideal approach for the delivery of various drugs in future.(64, 65)

S. No.	Drug Used	Objective	Indication	Reference
1	Terbinafine Hydrochloride	Formulation and Evaluation of Terbinafine Hydrochloride Emulgel	Fungal Infection	(66)
2	Ketoprofen	Preparation, Characterization, & Evaluation of Ketoprofen Emulgel	Anti-Inflammatory	(67)
3	Mefenamic acid	Formulation & Evaluation of mefenamic acid emulgel	Anti-Inflammatory	(44)
4	Chlorphenesin	Formulating & Optimizing of Chlorphenesin Emulgel	Anti-Fungal	(68)
5	Piroxicam	Formulation Design & Development of Piroxicam Emulgel	Anti-Inflamatory	(15)
6	Diclofenac	Development & optimization of novel Diclofenac emulgel	Anti-inflamatory	(57)
7	Clarithromycin	Development & Evaluation of Clarithromycin Emulgel	Broad spectrum antibiotic	(43)
8	Efavirenz	Formulation, Optimization & Evaluation of efavirenz emulgel	HIV Infcetion	(69)
9	Ketoconazole	Development & Characterization of ketoconazole emulgel	Anti-fungal	(70)
10	Ciprofloxacin	Formulation and In-Vitro Evaluation of Ciprofloxacin Loaded Topical Emulgel	Antimicrobial	(71)
11	Clotrimazole	Formulation & Evaluation of Clotrimazole Emulgel	Skin Infection	(72)
12	Thymol	Formulation & Characterization of Thymol containing nano-emulgel	Acne	(73)
13	Dexibuprofen-Capsaicin	Formulation Development, Characterization, & Evaluation of Dexibuprofen-Capsaicin Skin Emulgel	Anti-inflammatory & Analgesic Effects	(74)
14	Zolmitriptan	Preparation & evaluation of optimized zolmitriptan niosomal emulgel	Migraine	(75)

Table 1: List of Drugs being used in Previous Studies for Developing & Evaluating Emulgel

S. No.	Brand Name	Active Ingridient	Indication	Manufacturer	Reference
1	Voltaren Emulgel	Diclofenac Diethyl Ammonium	Osteoarthritis	Novartis Pharma	(76)
2	Miconaz H Emulgel	Miconazole nitrate, Hydrocortisone	Fungal Infection	Medical union Pharmaceuticals	(77)
3	Pernox gel	Benzoyl peroxide	Acne	Cosme Remedies Ltd	(78)
4	Clinagel	Clindamycin phosphate Allantoin	Acne & Pimples	Stiefel Pharma	(79)
5	Topinate gel	Clobetasol propionate	Dermatitis, Eczema, & Allergies	Systopic Pharma	(80)
6	Accent gel	Aceclofenac, Methyl salisylate,Capsaicin	Sensitivity & Plaque	Intra labs India Pvt Ltd	(8, 81)
7	Avindo gel	Azithromycin	Acne Vulgaris	Cosme Pharma laboratories	(8, 81)
8	Cloben gel	Clotrimazole, Beclomethasone Dipropionate, Neomycin	Skin Infections	Indoco Remedies	(82)
9	Zorotene gel	Tezarotene	Psoriasis & Acne	Elder Pharmaceuticals	(83)
10	Volini gel	Diclofenac Diethylamin, Methyl Salicylate, Menthol, Linseed oil	Muscle Pain, Strains, Sprains, Spasms, & Cramps	Ranbaxy Pharmaceuticals	(84)
11	Isofen Emulgel	Ibuprofen	Relieving Pain, Reducing Swelling & Easing Inflammation	Beitjala Pharma	(85)
12	Voltarol Emulgel P	diclofenac diethylammonium	Pain	GSK	(86)
13	Dosanec Emulsion Gel	Diclofenac diethylamine	Pain	Siam Pharmaceuticals	(81)

14	Diclomax Emulgel	Diclofenac diethylamine	Pain & Swelling	Torrent Pharma	(77)
15	Dermafeet Emulgel	Urea	Cracked Heels	Herbitas	(8, 81)
16	Cataflam Emulgel	Diclofenac diethylamine	Pain	Novartis	(87)
17	Denacine Emulgel	Clindamycin Phosphate	Acne & Inflammation	Beit Jala Pharmaceutics	(85)

Table 2: Marketed Emulgels with Active Ingredient, Indication & Manufacturer

S. No.	Title of Patent	Patent Number	Outcome	Reference
1	Topical composition	US20100286268A1	Emulgel of Diclofenac diethylammonium salt (Voltaren) has high skin penetration with high stability, therapeutic efficacy and fewer side effects.	(88)
2	Method for debonding of orthodontic metal brackets with eugenol emulgel	US10426576B2 & US11141242B2	The Emulgel of eugenol can be used for removing the metal brackets, metal braces and enamel surfaces of teeth	(89)
3	Cosmetic or dermatological preparations based on emulsifiers which are free from ethylene oxide and propylene oxide, for the preparation of microemulsion gels	US6468551B1	Method of developing microemulgel consisting of oil based discontinuous phase and aqueous based continuous phase using emulsifiers and crosslinking substances.	(90)
4	Gel-microemulsion formulations	US7064114B2	A composition of emulgel, which can be used as spermicidal method and also sd as antimicrobial formulation.	(91)
5	Composition for microemulsion gel having bleaching and antiseptic properties	US5336432A	Emulgel is prepared by using water and propylene glycol as aqueous phase and oil phase, which is stabilized by using one or more surfactants.	(92)

6	Treatment of burns	US20030187069A1	This patent involves the method of preparing emulgel for the management of burns	(93)
7	Emulsion gels for well servicing	US2801218A	Provides a stable composition for the preparation of emulgel.	(94)
8	Aqueous two-phase emulsion gel systems for zone isolation	US7703527B2	Method of preparing water-in-water emulsion containing polymers or oligomers, which is then used to develop of emulgel by removing one polymer.	(95)
9	Topical emulsion-gel composition comprising diclofenac sodium	US7732489B2	The patent is related to the formulation of diclofenac sodium containing emulgel in which complete dissolution of diclofenac is achieved.	(96)
10	Water-in-volatile silicone emulsion gel cosmetic	US6017546A	This patent is related to the water in volatile silicon based emulgel. It leads to formation of clear gel formulation due to similarity in the refractive index of aqueous and oily phase.	(97)
11	Methods of treatment utilizing topical emulsion-gel composition comprising diclofenac sodium	US8557870B2	The patent is related to the method of treating burns and inflammation using dislofenac sodium containing emulgel.	(98)
12	Protein emulsion gels and processes for their preparation	US20100119682A1	It involves the method of preparing emulgel of protein, which forms a heat set gel.	(99)
13	Methods of forming a bicontinuous intraphase jammed emulsion gel and uses thereof	US20200353436A1	This patent is based on the formulation of bicontinuous intraphase jammed emulgel.	(100)
14	Method for preparing high-water-content emulsion gel using oil gelling agent	US20180280296A1	In involves the method of developing high water content containing emulgel, which is stabilized by the emulsifier.	(101)

Table 3: Patents Related to the Composition, Preparation & Utilization Emulgel

Conclusion

The benefits of Emulgel as well as recent advancements in this segment are indicating towards the impact of this formulation in delivering a wide range of active constituents via topical route. The commercial success of available emulgel products is concluding that this approach has potential to replace most of the conventional systems for topical delivery of drugs and helps in achieving better absorption and bioavailability of drugs. In addition to this, emulgel has better drug loading ability and stability as compared to both the parent products i.e. emulsions and gels. Further, the introduction of nanotechnology will overcome the present limitations related to the emulgels and more superior formulations are believed to formulate by incorporating this technology. Along with this, the structure of skin is also supplementing the penetrating power of emulgel while the identification of new permeation enhancers is also believed to improve the therapeutic potential of drugs when administered as emulgel.

The inability of conventional therapy to deliver the lipophilic drugs via topical route has also generated an intense need of novel formulation and emulgels are currently fulfilling all the requirements and hence covering a wide range of indications. Therefore, all the present advantages as well as expected future advancements in emulgel are promoting its presence in clinical pipeline and it is emerging as an ideal alternative for the topical delivery of drugs and several drugs including antimicrobials, NSAIDs, anti-fungal agents etc. are believed to administer as emulgels in future.

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