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Emulgel: A Novel Strategy for Enhanced the Topical Drug Delivery

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Abstract: Background: The study of pharmaceutical science has developed through time and is now of greatest importance in the current battle against sickness. Research on the utilization of biomolecules, such as medicines and proteins, to cure disease has advanced significantly in recent years. To induce a localizing effect or cure dermatological conditions, doctors can prescribe pharmaceuticals directly to the skin using a topical drug delivery device. Gels have been used in both medical and cosmetic formulations, unlike other dosage forms. An emulsion that has been combined with gel is known as emulgel. Emulgel is a topical drug delivery technology that has a dual release control mechanism that incorporates both gel and emulsion. Objective: Drug distribution of hydrophobic substances via the skin is the main objective of emulgel. Emulgels exhibit a dual release control system, i.e., an emulsion and a gel. A traditional emulsion becomes an emulgel when a gelling ingredient is included in the water phase. Conclusion: They will also become the best way for mixing water-soluble gel bases with hydrophobic medications. In addition, a number of permeation boosters can boost the effect, making Emulgel a more effective topical medication delivery route than the ones now in use. It is possible to extend the use of emulgel to include analgesics, anti-inflammatory, antifungal, anti-acne, and different cosmetic compositions.
Keyword: Emulgel, analgesics, anti-inflammatory, antifungal, anti-acne.

I. INTRODUCTION

The study of pharmaceutical science has advanced progressively across time, becoming extremely relevant in today's fight against disease. An area of study that has advanced significantly in recent years is the use of biomolecules, such as medicines and proteins, to cure disease [1]. The human body receives medications in a variety of ways, including sublingual, parenteral, rectal, inhaler and oral. Although the oral route is regarded as the most convenient, it still has drawbacks such low solubility and absorption. Topical medication delivery systems may be an alternative in this situation. Topical administration eliminates issues with first pass metabolism, intravenous therapy difficulties, and stomach emptying time in addition to absorption-related concerns including various enzymes, pH changes, and stomach emptying time. It is still challenging to transfer medications through the skin due to the hydrophobic moiety of the topical gel drug delivery method [2, 3].

A topical drug administration system is a method of prescribing medications directly to the skin in order to produce a drug's localizing effect or treat dermatological illnesses [4]. Drug release that is regulated and maintained may be accomplished by topical administration. There is no risk of infection because it is a noninvasive method of medication administration. Dermatological skin care treatments come in a variety of formulations and consistencies, from liquid to powder, although semisolid preparations are the most widely used. Solutions, suspensions, emulsions, semisolids (such as foams, ointments, pastes, creams, and gels), solids, and sprays are the most typical examples of topical dosage forms [5, 6, 7]. When other medication delivery methods (such as oral, sublingual, rectal, and parental) are ineffective or when a local skin illness such a fungal infection exists, the topical drug delivery technique is typically employed. For local and systemic therapy, topical medication administration is a desirable approach. The easy accessibility and direct interaction with the skin as a target for diagnosis and therapy is a key component of dermatological pharmacology [8, 9, 10].

A. Advantages of Topical Dosage Form [10, 11,12]

1) Are beneficial for patients and simple to use.
2) Prevents variations between and among patients as well as swings in medication level by completely eliminating the preparation;
3) Allows for the simple cessation of pill use, if necessary.
4) Possess the capability of medication delivery to a precise location.
5) Compared to the buccal or nasal cavities, they offer a broad area of application.

6) Can stop GIT compatibility issues.
7) The administrator is not need to be knowledgeable.
8) Eliminate the risks and difficulties associated with intravenous therapy as well as the various absorption circumstances, such as pH fluctuations, the presence of enzymes, and stomach emptying time and first pass metabolism.

B. Disadvantages of Topical Dosage Form [13,14]

1) The medications may get denatured by skin enzymes.
2) Certain medications don't pass through the skin very well.
3) The medicine and/or excipients may cause skin rashes or contact dermatitis.
4) Large-particle drugs are difficult to absorb through the skin.
5) Potential of allergic responses. Can only be used for medications with very low plasma concentrations.

C. Classification of Topical preparation [15 , 16, 17, 18]

Topical Dosage Form			
Solid Dosage Form	Liquid Dosage Form	Semi-solid Dosage Form	Miscellaneous Dosa- -ge Form
Powder	Lotion	Ointments	Transdermal prepara- -tion
Aerosol	Liniment	Cream	
Plaster	Emulsion	Paste	
	Aerosols	Gel	
	Suspension	Jelly	
	Solution	Suppositories	

D. Factors affecting topical absorption of drug [19, 20, 21, 22]

The way that medications are absorbed is influenced by a number of factors. This is a list of a few of them.

1) *Physiochemical Factors*
a) Partition coefficient
b) Molecular weight (<500 Dalton)
c) Degree of ionization
d) Effect of vehicles

2) *Physiological Factors*
a) Skin thickness
b) Density of hair follicles
c) Density of sweat gland
d) Blood flow
e) Hydration of skin
f) Inflammation of skin
g) Type of skin
h) Skin pH
i) Lipid contents

E. SKIN

The biggest organ of the body, the skin is composed of water, protein, lipids, and minerals. Skin controls body temperature and guards against infections. Skin nerves enable you to experience emotions like heat and cold [23, 24].

The integumentary system, which includes your skin, hair, nails, sweat glands, and oil glands, is pronounced "in-TEG-you-MEINT-a- ree." The term "integumentary" refers to a body's skin [25].

F. Physiology of Skin

The main organ for Topical Drug Delivery System (TDDS) is the skin, and molecules can enter the skin through the stratum corneum, sweat ducts, or sebaceous follicle. A third of the blood that circulates through the body passes through the 2m2 surface area of adult skin. The human skin has 200–300 sweat ducts and 40–70 hair follicles. The pH range of human skin is 4 to 5.6[27, 28, 29, 30]

G. Function of Skin: [31, 32, 33,34]

1) Protection: The skin is the body's primary physical defense against the outside world, providing defense against pathogens, dehydration, UV radiation, and mechanical harm.
2) Formation of Vitamin D: The ultraviolet light from the sun converts lipid base substance in skin (dehydrocholesterol) to vitamin D.
3) Regulation of body temperature: Skin contributes to thermal control by storing or releasing heat and aids in preserving the body's homeostatic and water balance. The important function of sin is thermoregulation
4) Absorption: Transdermal patches, e.g. Hormone replacement therapy, nicotine etc.
5) Excretion: Sodium chloride in sweat, aromatic substances, e.g. Garlic etc. excreted by skin.
6) Exocrine activity: The discharge of water, urea, and ammonia causes this to happen. Sebum, perspiration, and pheromones are all secreted by the skin, and it also performs crucial immunologic tasks by secreting bioactive molecules like cytokines.

H. Classification of Skin layers [35, 36]

Skin layers may be classified into three parts:

1) Epidermis: The stratified epithelium that makes up the skin's epidermis, which is made up of the following five layers, forms the epidermis.
a) Stratum corneum/horny layer: The top layer, which has 20–30 cell layers, is composed of keratin and horny scales comprised of defunct keratinocytes or anucleate squamous cells. The thickness of this layer fluctuates the greatest, notably in callused skin. The dead keratinocytes in this layer release immunoglobulins which are a component of our first line of immunological protection.[37]
b) Stratum Lucidum: This layer of cells is made up of flattened epithelial cells. Some cells lack a nucleus, while others may have a degraded nucleus. The stratum Lucidum (lucid = clear) is a region where cells have a glossy appearance and appear to be uniformly transparent.
c) Stratum Granulosum: A thin layer called the stratum granulosum has 2 to 5 rows of flattened rhomboid cells. The cytoplasm includes keratohyaline, a protein that serves as the building block for keratin.
d) Stratum Spinosum: The prickle cell layer, which is composed of 8–10 cell layers, is characterized by irregular, polyhedral cells with cytoplasmic processes often referred to as "spines" that extend outward and make desmosome-mediated contacts with nearby cells. This layer contains dendritic cells.
e) Stratum Germinativum: A thick layer where cells constantly divide through mitosis and travel toward the stratum corneum. Several projections from this layer descend into the dermis and serve as anchors and as food sources. The layer of skin that contains melanin determines the color of the skin.[38]

- *Cells of the Epidermis [39, 40, 41, 42]*

➢ Keratinocytes: The majorities of epidermis cells, known as keratinocytes, are found in the basal layer and generate keratin as well as lipids that help to construct the epidermal water barrier. When cholesterol precursors are activated by UVB radiation to produce vitamin D, keratinocytes also control calcium absorption.

- Melanocytes: The main product of melanocytes, which are descended from neural crest cells, is melanin, which gives skin its colour. They generate melanin and are situated between stratum basale cells. As a built-in sunscreen, UVB light induces the release of melanin, which protects against UV radiation. Tyrosinase, an enzyme, converts tyrosine to DOPA, which results in the production of melanin. The lengthy processes connecting the melanocytes to the nearby epidermal cells are then used to transport melanin from one cell to the next. Long processes carry melanin granules from melanocytes to the cytoplasm of basal keratinocytes. By "pigment donation," melanin is transmitted to nearby keratinocytes; this process includes keratinocytes phagocytosing the tips of the melanocyte processes.
- Langerhans' cells: Dendritic cells, also known as Langerhans cells, are the skin's first line of defense and are crucial to antigen presentation. To see these cells, which are mostly present in the stratum Spinosum, specific stains are required. These cells come from CD34-positive bone marrow stem cells and are of mesenchymal origin. They are a component of the mononuclear phagocytic system. They include tennis racket-shaped cytoplasmic organelles called Birbeck granules. Both MHC I and MHC II molecules are expressed by these cells, which also take up cutaneous antigens and transport them to the lymph node.
- Merkel Cells: Oval-shaped modified epidermal cells known as merkel cells are located in the stratum basale, right above the basement membrane. These cells, which are mostly located in the fingers but are also present in the palms, soles, oral mucosa, and vaginal mucosa, have a sensory role as mechanoreceptors for mild touch. Their membranes interact with free nerve endings in the skin and they are connected to neighboring keratinocytes by desmosomes. They also include intermediate keratin filaments.

Your epidermis is the top layer of the skin that you can see and touch. Keratin, a protein inside skin cells, makes up the skin cells and, along with other proteins, sticks together to form this layer. The epidermis layers do: [43]

- Acts as a protective barrier: Infection-causing bacteria and germs are prevented from getting into your body and bloodstream by the epidermis. In addition, it shields from the sun, rain, and other elements.
- Makes new skin: Skin cells are continuously produced by the epidermis. Your body eliminates around 40,000 old skin cells every day, which are replaced by these new ones. Every 30 days, your skin is renewed.
- Protects your body: The epidermis contains Langerhans cells, which are a component of the immune system. They aid in the battle against diseases and bacteria.
- Provides skin color: Melanin, the pigment that gives skin its color, is found in the epidermis. The color of your skin, hair, and eyes depends on how much melanin you have. Individuals with darker skin and those who produce more melanin may tan more quickly.

2) Dermis: The dermis is under the epidermis and is distinguished by having a lot of elastin fibers, which give skin its ability to stretch, as well as a lot of collagen, which gives skin its strength. Dermal blood vessels deliver nutrition to the dermis and epidermis. Dermis also plays a major role in temperature regulation. Dermis has a thickness of 3-5mm. The dermis, which makes up the majority of the skin, is responsible for its flexibility, elasticity, and toughness. It binds water and shields the body from mechanical harm. Involves sensory stimulus receptors and assists in regulation. There are two distinct types of dermis:

a) Superficial Papillary Layer: The epidermis contains this papillary dermis.. Blood arteries, lymphatic, elastic fibers, and a bag of collagen are loosely distributed in this layer. Chromatophores, a kind of cell, are also present in this layer.

b) Reticular Layer: This layer is composed of elastic and reticular fibers. The reticula layer is made up of thick elastic fibers, deep epidermal appendages, dense collagen fibers, and vascular and nervous systems. Around the hair bulbs, sweat glands, and sebaceous glands are elastic fibers. The dermis makes up 90% of skin's thickness. The middle layers of skin do:

- Has collagen and elastin: Collagen is a protein that makes skin cells strong and resilient. Another protein found in the dermis, elastin, keeps skin flexible. It also helps stretched skin regain its shape.
- Grows hair: The roots of hair follicles attach to the dermis.
- Keeps you in touch: Nerves in the dermis tell you when something is too hot to touch, itchy or super soft. These nerve receptors also help you feel pain.
- Makes oil: The dermis contains oil glands that keep the skin supple and smooth. When you swim or are trapped in a downpour, oil also helps to keep your skin from absorbing too much water.
- Produces sweat: Dermal sweat glands produce sweat, which is released through skin pores. Your body temperature may be controlled by sweat.

- Supplies blood: Sweat from dermal sweat glands escapes through skin pores. Sweat may regulate the temperature of your body.[43]

3) *Hypodermis:* The skin's hypodermis is its deepest layer. It is the layer that lies between the skin and the body's internal organs and bones and muscles. The epidermis is home to sweat glands, sebaceous glands, and hair follicles, but the dermis is where they originate. All across the body, sweat glands release a watery salt solution onto the skin's surface. The fluid evaporates, cooling the skin and controlling temperature. The sebaceous glands secrete sebum, an oily substance that serves as a waterproof coating and prevents both hair and skin from drying out. The bottom layer of skin, or hypodermis, is the fatty layer. The hypodermis layers do:

a) Cushions muscles and bones: Muscles and bones are shielded from harm by fat in the hypodermis when you fall or get into an accident.

b) Has connective tissue: This tissue connects layers of skin to muscles and bones.

c) Helps the nerves and blood vessels: In the hypodermis, the dermis's middle layer's nerves and blood vessels enlarge. The hypodermis is connected to the rest of the body via branching nerves and blood arteries.

d) Regulates body temperature: Fat in the hypodermis keeps you from getting too cold or hot [43]

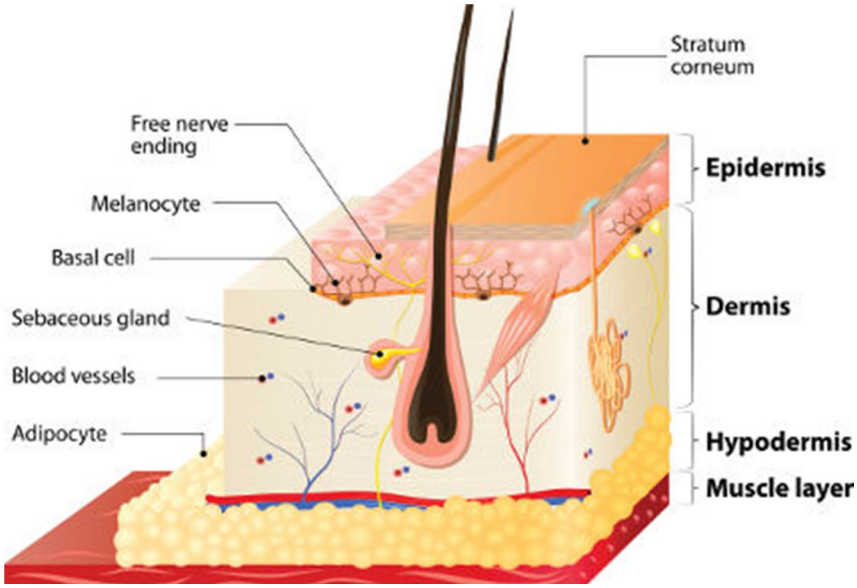

Figure no 1: Structure of skin [44, 45]

I. Drug delivery across the skin

The skin has two significant layers. Dermis and epidermis are what they are. The subcutaneous layer of the skin has a profusion of blood vessels. Three main mechanisms—transcellular, follicular, and transcellular—are involved in medication absorption via the skin. The intercellular matrix tends to be permeated by the pilosebaceous route, which is the second most typical route of delivery, although it has been demonstrated that the transcellular pathway offers a quick alternate route for highly polar compounds. It has been discovered that the keratinized corneocytes and the predominantly non-polar lipid intercellular cement of the horny layer are the key components involved in the preservation of an effective barrier for medications in normal, healthy, or undamaged skin. [46]

J. Permeation Of The Drug Through The Skin

The skin develops waterproof layers that shield the underlying, more fragile tissues. Dermis and epidermis, two significant skin layers, are present. The epidermis is made up of stratified keratinized epithelium, which varies in thickness depending on where on the body it is located. It is the layer of skin that is closest to the surface. There is no blood flow in the layers of the epidermis, which range in thickness from 100 to 150 m. Stratum corneum is a layer that makes up the epidermis. The stratum corneum is composed primarily of keratinocytes that are dead and dehydrated and has a thickness of 10 to 15 m. Transcellular, intercellular, and follicular are the three methods of topical medication absorption. Pilosebaceous distribution is the most typical medication delivery method. The Transdermal medication delivery system is designed around the reservoir and matrix ideas.

Both processes require drug dispersion via the skin. the capacity of chemical enhancers to be tolerated by skin and the enhancing effect necessary for the transport of macromolecules with poor permeability coefficients. The addition of permeation enhancers, such as fatty acids, surfactants, esters, and alcohols, which modify the formulation's excipients and temporarily alter the stratum corneum's barrier properties through a variety of mechanisms including improving solubility, partitioning the stratum corneum, fluidizing its crystalline structure, and dissolving stratum lipids increases drug flux.

The delivery of medication and antibiotics to an afflicted place of the body has long been accomplished with the use of creams and gels that are applied to the skin. Now, thanks to new technology, it is possible to absorb additional medications via the skin. Not only the damaged parts but the entire body can be treated with them. [47, 48]

II. EMULGEL

In comparison to other dosage forms, gels have been utilized in both medicinal and cosmetic formulations. Emulgel is the name for an emulsion that has been mixed with gel. Emulgel, which features a dual release control system that includes both gel and emulsion, is a topical medication delivery device [49]. Two types of topical delivery products are available. They are external and internal products. As their name indicates, the external products are applied by spreading or spraying, and the internal products are applied orally, vaginally or rectally [50].Emulgels are advantageous for usage in dermatology because to their thixotropic, ease of spreading and removal, ease of emollient application, non-stinging nature, extended shelf life, transparency, and appealing look. This study covers emulgel, its benefits, qualities, formulation concerns, and most current developments in the field of research [51].

Emulgels are essentially w/o or o/w emulsions that have been mixed with a gelling agent to create a gelled state. Emulgels are the most stable and ideal delivery system for hydrophobic medicines. Emulgels have a high rate of patient acceptance since they combine the benefits of both gels and emulsions [52]. Emulgels function as two different controlled release methods since they combine the qualities of an emulsion and a gel (Fig.2). Emulgels, which have two phases aqueous and non-aqueous can, deliver both hydrophilic and lipophilic medicines. Emulgels are applied efficiently on the skin since they are non-greasy in comparison to other topical medicines that require excessive rubbing for Spreadibility [53]. The surface tension between a colloid's normal 99% weight of liquid and a macromolecular network of fibers constructed from a little quantity of gelatin material makes up a gel. Despite numerous benefits, delivering hydrophobic medicines remains a significant barrier. In order to overcome this limitation, an emulsion-based technique is being employed to successfully integrate and distribute a hydrophobic medicinal component via emulgels [54, 55]. The emulgel preparations are significantly more stable than other types of topical preparations like powder, which may be hygroscopic and absorb moisture when it is directly exposed to the environment, creams, which exhibit phase inversion, and ointments, which exhibit rancidity because of oil base. Emulsions are readily removed whenever wanted and have a certain level of elegance. They are highly capable of penetrating the epidermis. Emulgels for skin use have a number of advantageous qualities. Emulgels are now used to address a variety of skin conditions, including those caused by bacterial, viral, and fungus species. (Acne, eczema, Herpes simplex).Different scientists have conducted studies on the antifungal medications added to emulgel to evaluate its effectiveness against fungus infections like candidiasis. Candida tropicalis, Candida albicans, Candida parapsilosis, Candida glabrata, and Candida krusei are the species that cause candidiasis. It was discovered that creating the emulgels was effective in battling the fungus. To address a variety of skin conditions, scientists have been working to create medication emulgels [55, 56].

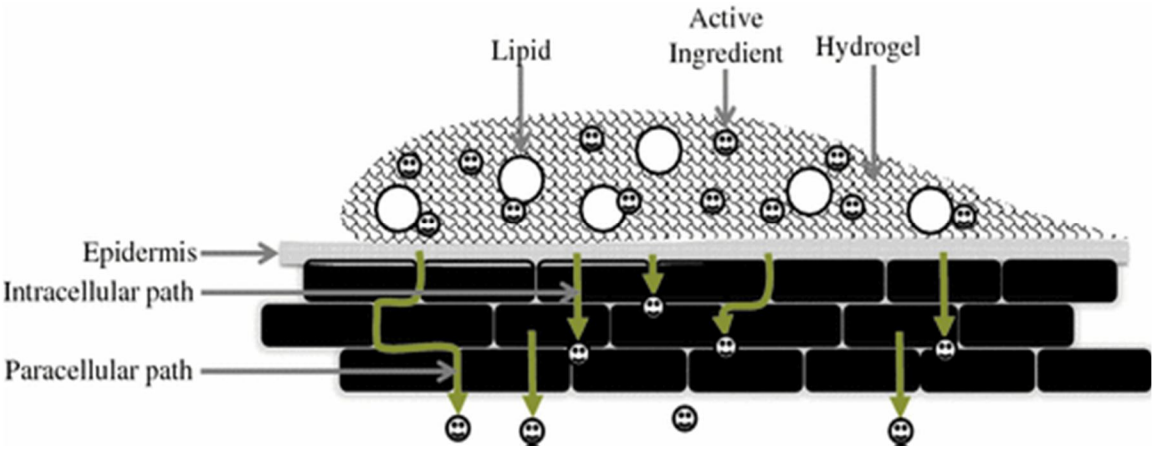

Figure No 2: Structure of Emulgel [57].

A. Types of Emulgel [58, 59,60]

1) *Micro Emulsion:* Micro emulsions are thermodynamically stable, optically transparent mixes of a biphasic o/w systemic stabilized with a surfactant. Droplets don't agglomerate and range in size from 10 to 100nm. It contains specified quantities of water, surfactant, co-surfactant, and oil. Extremely low interfacial tension, a wide interfacial area, and the capacity to dissolve both aqueous and oil-soluble substances are just a few of the special qualities that micro emulsions may possess. Because the stratum corneum's diffusion barrier is lowered by the components of micro emulsion, the medicine may penetrate the tissue more quickly. Micro emulsions have a low skin retention capacity because to their low viscosity, which limits their usage in the pharmaceutical sector.
2) Nano emulgel: A transparent oil-water dispersion known as a nanoemulsion is thermodynamically stable because it contains molecules of cosurfactant and surfactant with globule sizes ranging from 1 nm to 100 nm. The word Nanoemulgel is used when the emulsion and gel are combined. Comparing Nanoemulsion to more conventional formulations like emulsions and gels, several medicines exhibit increased transdermal penetration. The Nanoemulsion has improved transdermal and dermal distribution capabilities both in vivo and in vitro. Due to its tiny globule size and high loading capacity, the medication readily enters the skin and has a short-lived therapeutic impact.
3) Macro emulsion gel: Emulgel that contains emulsion droplets with a particle size higher than 400 nm. The individual droplets are not visible to the naked eye, yet they are plainly apparent under a microscope. Surface-active substances can aid in stabilizing macroemulsions, which are thermodynamically unstable.

B. Advantages of Emulgel [60, 61]

1) Hydrophobic drug can be easily incorporated by using o/w emulsion.
2) Better stability.
3) Better loading capacity.
4) Low preparation cost.
5) Prolonged effect of drug (controlled release).
6) Improve patient compliance.
7) Avoidance of first pass metabolism.
8) Self-applied medication.
9) Termination of therapy when required.
10) Suitable for drug with short half-life and for potent drug.
11) Site specific drug delivery system.
12) Avoidance of gastrointestinal incompatibility

C. Disadvantages of Emulgel [62, 63]

1) Contact dermatitis and skin irritability.
2) The potential for allergic responses.
3) The inadequate epidermis absorption of some medications.
4) It is difficult for drugs with big particle sizes to pass through the epidermis.
5) The occurrence of the bubble during formulation of emulgel.

D. Properties of Emulgels [64]

Properties	**Criteria**
Effective concentration	less than 10 mg
$t_{1/2}$	≤10 hr.
Molecular mass	800 Dalton or less; desirably 500 Dalton or less
log *p* value	0.8 to 5
Skin permeability coefficient	≥ 0.5 x 10-3 cm/hr.
Irritation to skin	Non-irritating
Polarity	Less
Molecular size	Small

E. Method &Material Of Preparation For Emulgel

Gel and emulsion are combined to create emulgel. Both the emulsion and the gel are made separately and combined. Aqueous and oil phases are taken separately and combined to create an emulsion. After that, a gelling agent is used to prepare the gel. Gel and emulsion are prepared, and then they are combined with moderate stirring. Castor oil, clove oil, liquid paraffin, and other compounds are employed as the oil phase. As an aqueous phase, water and alcohol are utilized. [65]

The drug is dissolved in ethanol, and the two phases are combined with constant stirring to create the aqueous and oil phases, respectively. Next, the polymers are dissolved in water with a pH range of 6.0 to 6.5, and the emulsion and gel are prepared separately and combined to create the emulgel. [66]

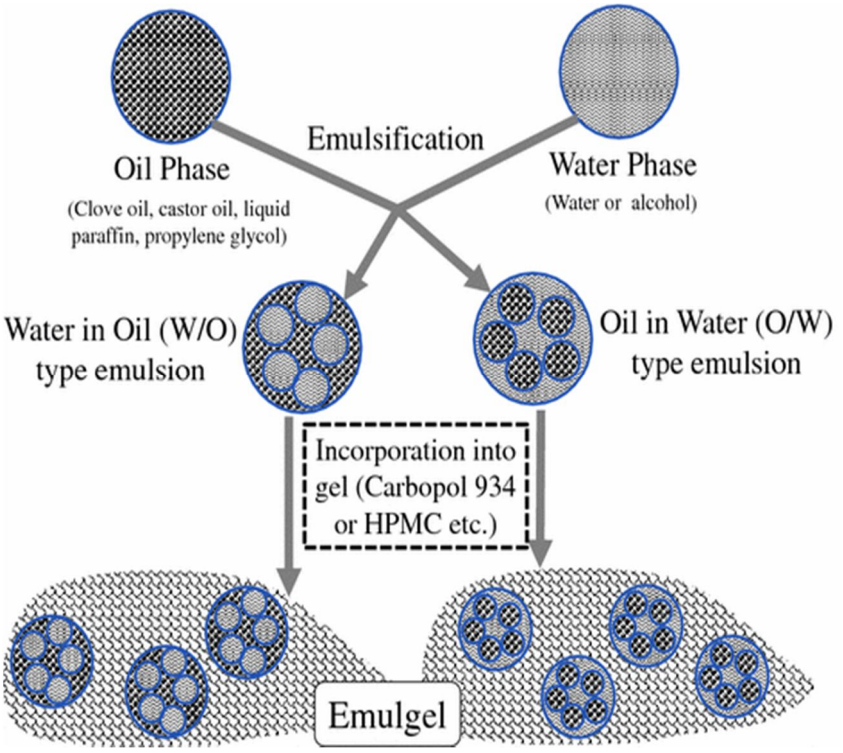

Figure No3: Method of preparation [67]

F. Important Constituents For The Preparation Of Emulgel

1) Vehicle

As the composition of the vehicle may significantly affect the pace and amount of absorption, comprehensive pharmaceutical research has demonstrated that the vehicle is a key connection between medication potency and therapeutic efficacy. In other cases, substances in the vehicles, such humectants, which have a strong affinity for water, may dry the stratum corneum and reduce penetration. They also have an impact on medication absorption by causing skin surface water vapor to evaporate [68]. The vehicle has the following characteristics:

a) During distribution, place the medicine on the skin.
b) Drug migration at the site of action is unrestricted.
c) Send the medication to the desired location and keep it there.
d) Specifically developed to address the anatomic spot being treated.

- *Aqueous Material*

The aqueous phase of an emulsion is formed by aqueous material. Water and alcohols are among the often utilized substances [69].

- *Oils*

The oily phase of the emulsion is formed by oils. Fish liver oils, different fixed oils of vegetable origin, non-biodegradable mineral castor oils that have a local laxative action, and other topically applied emulsions [70, 71].

Quantity of vehicles used in Emulgel

Chemicals	Quantity	Dosage form
Light liquid paraffin	7.5 %	Emulsion and Emulgel
Isopropyl palmitate	7-7.5 %	Emulsion
Isopropyl stearate	7-7.5 %	Emulsion
Isopropyl myristate	7.7.5 %	Emulsion
Propylene glycol	3-5 %	Gel

2) Emulsifier

The main purpose of an emulsifying agent is to facilitate the emulsification of oil and water during formulation. They make the emulsion more stable and extend its shelf life, which for commercial preparation might range from days to months or years. This delays the emulsion's phase separation. As emulsifying agents, sorbitan monooleate (Span 80), polyoxyethylene sorbitan monooleate (Tween 80), stearic acid, and sodium stearate are the main ingredients in emulgel [71, 72].

3) Gelling Agents

These substances are used to create gel bases so that emulsion may be added to them to create Emulgel. By expanding in the aqueous phase and forming a gel-like structure, gelling agents are used to enhance the consistency of any dosage form. They are utilized in Emulgel as a thickening agent [73, 74]. Below are provided some instances of gelling agents.

Gelling agents	Quantity	Dosage form
Carbopol-940	1 %	Emulgel
Carbopol-934	1 %	Emulgel
HPMC-2910	2.5 %	Emulgel
Sodium CMC	1 %	Gel
HPMC	3.5 %	Gel

4) Penetration Enhancers

These are the substances that are utilized to boost a drug's ability to penetrate the skin. They facilitate drug absorption through the skin and momentarily disturb the stratum corneum skin barrier's highly organized structure, fluidize the lipid channels between corneocytes, change how the drug is partitioned into the skin's structures, or improve skin delivery. Penetration Enhancer used in Emulgel [75, 76].

Penetration Enhancer	Quantity	Dosage form
Oleic acid	1 %	Emulgel
Linoleic acid	5 %	Gel
Urea	10 %	Gel
Lecithin	5 %	Gel
Isopropyl myristate	5 %	Gel
Clove oil	8 %	Emulgel

G. Ideal Properties Of Additives

1) They should be nontoxic.
2) They should be easily available.
3) They should be cheap.
4) They do not be contraindicated.
5) They should chemically and physically be stable. [77]

H. Packaging Of Emulgels

Emulgels are packaged in either an aluminum laminated tube with a moulded seal and a propylene screw cap, or in an aluminum tube with a membrane seal and an interior coating of phenoxy-epoxy lacquer.

Materials for tubes with laminates

1) Laminated foil

It offers a barrier against light, air, and moisture.

2) All laminated plastic

It features a barrier that resists chemicals. [78]

I. Marketed Formulation

Sr. No.	Brand Name	Active Ingredient	Manufacture
1.	Adwiflam Emulgel	Diclofenac diethylamine, Methyl Salicylate &Menthol	Saja Pharmaceuticals
2.	Avindo Gel	Azithromycin	Cosme Pharmaceuticals
3.	Benzolait emulgel	Benzoyl Peroxide &Biguanide	Roydermal
4.	Cataflam Emulgel	Diclofenac Potassium	Novartis
5.	Diclomax Emulgel	Diclofenac Sodium	Torrent Pharmaceuticals
6.	Dermafeet Emulgel	Urea	Herbitas
7.	Diclona Emulgel	Diclofenac Diethylamine	Kuwait sauid pharmace- - ticals
8.	Diclon Emulgel	Diclofenac Diethylamine	Med Pharma
9.	Dosanac emulsion gel	Diclofenac Diethylammonium	Siam Bheasach
10.	Denacine Emulgel	Clindamycin Phosphate	Beit jala Pharmaceutical
11.	Isufen Emulgel	Ibuprofen	Beit jala Pharmaceutical
12.	Miconaz-H-Emulgel	Miconazolenitrate ,Hydrocotiso--ne	Medical Union Pharmac- - euticals
13.	Nucoxia Emulgel	Etoricoxib	Zydus Candila Healthca- -re LTD
14.	Voltarol Emulgel	Diethylammonium	Novartis
15.	Voltaren Emulgel	Diclofenac Diethylammonium	Glaxo Smithh Kine
16.	Volini Gel	Diclofenac Diethylamine	Ranbaxy Laboratories
17.	Excex gel	Adapalene, Clindamycin	Zee laboratories
18.	Clinagel	Allantoin, Clindamycin Phosph- ate	Stiefel Pharma
19.	Nadicin cream	Nadifloxacin	Psychoremedies
20.	Acent gel	Capsaicin, Aceclofenac, Methyl salicylate.	Intra labs India Pvt Ltd
21.	Lupigyl gel	Metronidazole	Lupin Pharma
22.	Kojivit gel	Octinoxate, Kojicacid, Dipalmit- ate Arbutin	Micro Gratia Pharma
23.	Zortene gel	Tezarotene	Elder Pharmaceuticals
24.	Cloben gel	Neomycin, Clotrimazole, Beclomethasone dipropionate	Indoco Remedies
25.	Topinate gel	Clabetasol propionate	Systopic Pharma

J. Evaluation Test For Emulgels

1) Physical Determination: The prepared emulgel color, consistency, homogeneity, and phase separation were all visually assessed.[79]

2) pH determination: Using 1% w/v aqueous solutions of the generated Emulgel, the pH values of the Emulgel formulation were measured using a digital meter. Emulgel was dissolved in 100 ml of distilled water with one gram added, and the mixture was left for two hours. Each formulation's pH was measured three times, with the average value being computed.[80]

3) Spreadability study: The spreadability coefficient was to be calculated using Mutimer's specified equipment. The device consists of a wooden block with a pulley attached to one end. Based on the prepared Emulgel's "Slip" and "Drag" properties, the spreading coefficient was calculated. The hook came with a ground glass slide that was the same size as the fixed ground slide. To remove air and establish a consistent coating of Emulgel between the two slides, a weight of 20 grams was placed there for five minutes. A certain amount of weight was added to the pan, which was hooked to the pulley. It was observed how long (in seconds) it took for the top slide to disengage from the bottom slide [81]. The spreadability is calculated by using the Formula.

$$S = M.L/T$$

Where M= wt. tied to upper slide.
L= Length of glass slide.
T= Time taken to separate the slides

4) Rheological study: At a temperature of 37°C, the viscosity of the produced Emulgel was measured using a digital viscometer. The mixture was poured to the beaker. Spindle number III was dropped perpendicularly into the center of the emulgel, being careful not to let the spindle hit the bottom of the jar. The spindle was spun between 10 and 100 times per minute, and the viscosity was recorded [82].

5) Drug content determination: The spectrophotometric approach was used to determine the drug concentration in Emulgel. By sonicating 1 g of Emulgel in 100 ml of solvent, the drug concentration of Emulgel was calculated after sonicating and filtering the stock solution, aliquots of various concentrations were made, and absorbance was measured by using a UV-VIS spectrophotometer. Equation derived by calibration curve linear regression analysis was used to determine drug content [83].

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

6) Swelling Index: A 50 ml beaker containing 10 ml of 0.1 N NaOH and 1 g of the manufactured topical emulgel are used to individually measure the swelling index of the gel. At various time intervals, samples were taken out of the beakers and placed on a dry surface before being reweighed. The formula used to compute the swelling index is

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

Where, (SW) % = Equilibrium percent swelling,
Wt = Weight of swollen Emulgel after time t,
Wo = Original weight of Emulgel at zero time [83].

7) Stability Studies: The produced emulgels were placed in aluminum collapsible tubes (5 g), and stability tests were conducted on them for three months at 5°C, 25°C/60% RH, 30°C/65% RH, and 40°C/75% RH. Samples are taken out after 15 days and assessed for their physical attributes, pH, rheological characteristics, drug content, and drug release patterns [84, 85].

8) Microbiological assay: This strategy takes advantage of the ditch plate technique. By using this technique, the activity of bacteria or fungus is determined [86].

9) Skin irritation study: Due to the topical formulation of the medication, this test is particularly significant. The test is conducted on an animal's skin. The preparation of emulgel is weighted or applied to a rat's or rabbit well shaved skin, and any adverse reactions, such as a change in skin color or morphology, should be monitored for up to 24 hours. The study can employ the entire set of 8 rats. The test is considered successful if there is no irritation. The trial should be repeated if the skin irritation symptom appears in more than two animals [87].

10) Ex vivo skin permeation studies: The male rats can be used to conduct the ex vivo skin permeation research. The entire thick abdomen skin is cut off, maintained hydrated for an hour, and then put on a Franz diffusion cell. The emulgel is placed on the Franz diffusion cell after being glued to the skin. The medium is contained in the receptor compartment, which is constantly agitated. The aliquots are removed and spectrophotometric estimates are made [88].

K. List of Patent [89]

Sr. No.	PATENT NO	Year	INVENTORS	TITLE OF PATENT
1.	EP2214642 A1	2010	Fabienne Caillet- Bois, Isabel- -le Rault, Michel Steiger	Topical composition

2.	EP2019666 A2	2009	Cristina Cavallari, Barbara Luppi, Pietra Anna Maria Di, Lorenzo Rodirgu	Pharmaceutical prepar- - ations for transdermal use
3.	2007129162	1999	Cristina Cavallari, Barbara Luppi, Pietra Anna Maria Di, Lorenzo Rodirguez	Pharmaceutical prepar- - ations for transdermal use
4.	WO2002017905 A2	2002	Ancerewicz Jacek, Kienzler Jean-Luc, Sallin Dominique, Schumann Phyllis	Treatment of burns
5.	US 6004566 A	2007	Doron Friedman, Joeph Schwartz, Haim Aviv	Topical and transdemr- -al delivery system util--izing submicron oil sp- -heres
6.	5639738x	1995	Falk, Rudolf Edgar, Asculai, Samuel Simon	Topical composition containing hyaluronic acid and NSAIDs

III. CONCLUSION

Following a careful review of the literature, we came to the conclusion that emulgels are the most practical, superior, and efficient delivery method. In comparison to other topical drug delivery systems, it offers greater drug release since it is non-greasy, gel-like, and lacks oily bases. Gel becomes a dual control release system when emulsion is added, which solves issues with emulsion creaming and phase separation while also enhancing stability. Emulgel is a promising medication delivery strategy in the field of dermatology since it has been shown to be beneficial in treating several cutaneous conditions. Several hydrophobic medications are mixed with oily bases and applied to the skin using emulgel. Emulgels have an advantage in terms of extrusion, viscosity, adhesion, and spreadability. Also, they will develop into the ideal method for adding hydrophobic medicines to gel bases that are water soluble. Other than that, several permeation enhancers can increase the impact, making Emulgel a superior topical drug delivery method to the ones already in use. Emulgel's application can be broadened to include analgesics, anti-inflammatory, antifungal, anti-acne, and various cosmetic formulations.

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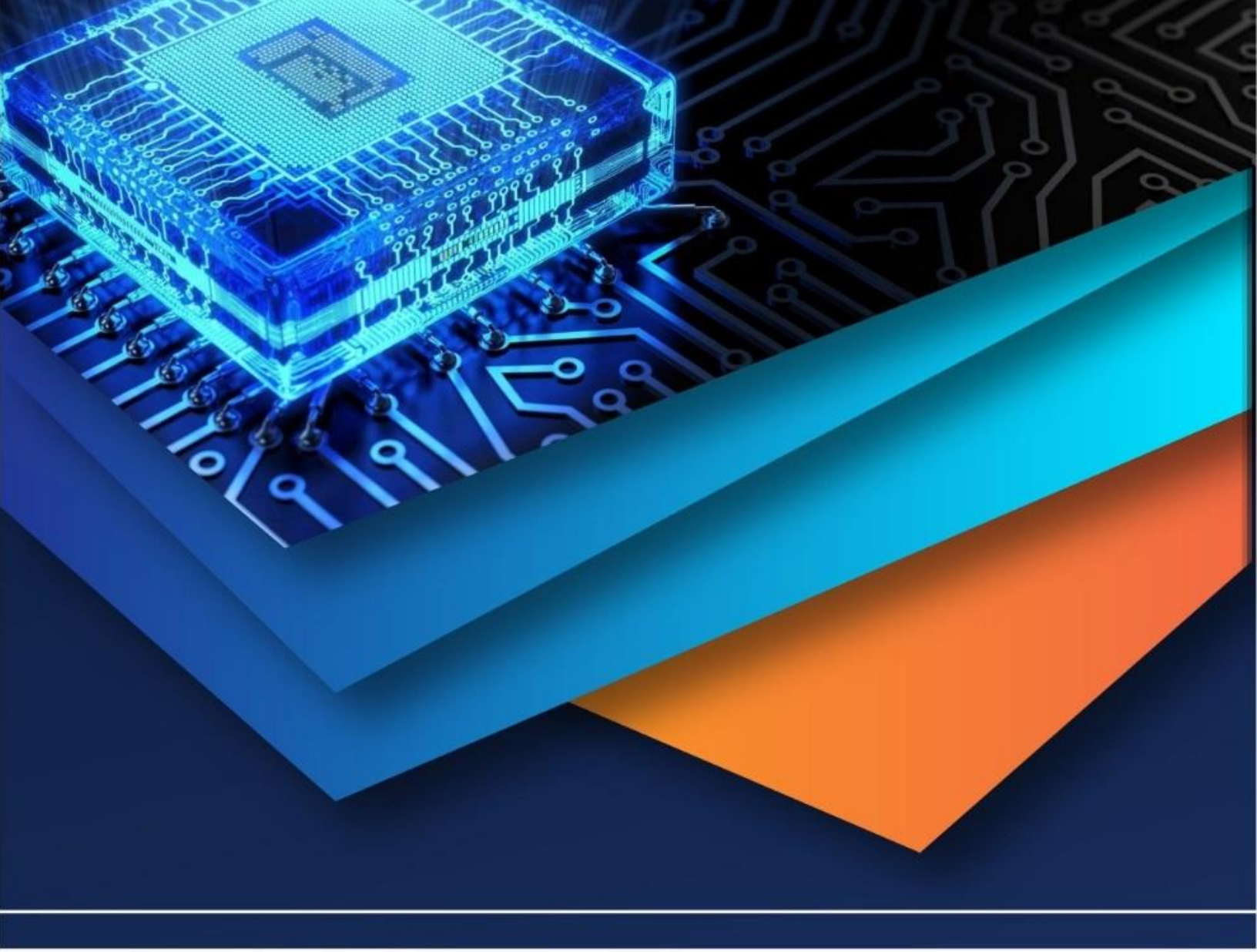

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