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Emulgel: A Reviewj

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ABSTRACT
Emulgel is used to treat colds, headaches, muscle aches, backaches, arthritis, and other diseases and injuries that produce aches and pains. Topical drug delivery, Emulgel, Gelling agents, Skin disorders In chronic skin illnesses such as fungal infections, acne, and psoriasis, patient adherence to topical formulations is critical. Emulgel is a new technology in NDDS that is utilised topically and has dual control release properties, i.e. emulsion and gel. Emulgels, which contain a dual release control mechanism (gel and emulsion),have become one of the most fascinating topical delivery technologies. The dosage form is referred to as emulgel when emulsion and gel are joined

I. INTRODUCTION

The application of a drug-containing formulation to the skin to treat a cutaneous disorder directly is known as topical drug delivery.The topical medication delivery technique is typically employed when other routes of drug delivery are unavailable. When oral, sublingual, rectal, or parental administration of medicine fails or is inefficient,[1] A fungal infection that appears to be localised on the skin. A topical delivery system's main benefit is that it avoids first-pass metabolism. Avoiding intravenous therapy's risks and drawbacks, as well as the various types of intravenous therapy-absorbing circumstances, such as pH shifts and stomach emptying time. When other methods of drug administration fail, the topical drug delivery system is typically used. The research is also being done to avoid any potential dangers. IV therapy and the various intravenous therapy conditions are inconvenient. Absorption is influenced by pH changes, enzyme presence, and gastrointestinal transit. It's time to clean out the refrigerator.

The simplest and most convenient method of localised drug administration is topical drug administration. Drug delivery to any part of the body via ocular, rectal, and other channels [2]. The formulations are available in a variety of forms, including solid, semisolid, and liquid. Drugs can be applied topically to have an effect at the application site or systemically. Absorption of drugs is a complicated process. It is possible to enhance a drug substance that is in solution and has a high molecular weight through the skin. If it's a non-electrolyte, the lipid/water partition coefficient will be favourable. Topical treatments can be used on the skin, which is one of the most accessible areas of the body. The skin is penetrated the most by three types of administration and molecules. The sebaceous follicle travels through the epidermis, sweat ducts, and a healthy stratum conium. Topical drug delivery via ophthalmic, rectal, vaginal, and skin routes is used for localised action on the body. Topical drug delivery systems like emulgel (gellified emulsion) are commonly used when other drug delivery systems fail to treat cutaneous disorders like fungal infections, acne, psoriasis, and so on [3]. Emulsion gels have become increasingly important in the field of pharmaceutical semisolid dosage forms since the mid-1980s. They're a hybrid of a gel and an emulsion, as the name implies.

EMULGEL 1-4

Drugs are delivered to the skin using emulsions of the oil-in-water and water-in-oil types. They can also penetrate the skin very well. When the gelling agent is present in the water phase of a traditional emulsion, it transforms into an emulgel. Thixotropic, greaseless, readily spreadable, easily removable, emollient, non-staining, water-soluble, longer shelf life, bio-friendly, clear are some of the benefits of emulgel for dermatological application, and pleasing appearance. Molecules can enter the skin through the intact stratum corneum, sweat ducts, or sebaceous follicle.

On the stratum corneum's surface, more than 99 percent of the total skin surface is available for percutaneous drug absorption. The ability of percutaneous absorption to pass through this outermost layer is limited. The creation of a concentration gradient, which provides the driving force for drug movement across the skin, the

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release of drug from the vehicle (partition coefficient), and drug diffusion through the layers of the skin are the primary phases in percutaneous absorption (diffusion coefficient).

Advantages [5, 6]

1. There is no such thing as a first-pass metabolism.
2. There is no gastrointestinal tract incompatibility.
3. Increased focus on a single location.
4. Increase patient adherence.
5. Self-medication suitability
6. Allowing the use of drugs with a short biological half-life.

A small therapeutic window exists.

7. The ability, if necessary, to stop taking medication as soon as possible.
8. It's simple and convenient to use.
9. Drugs that are hydrophobic are included.
10. Increased capacity for loading
11. Stability improvements.

Disadvantages

1. Skin irritation is a symptom of contact dermatitis.
2. There's a chance of allergic reactions.
3. The skin permeability of some drugs is low.
4. Skin absorption of large-particle drugs is difficult.
5. The formation of a bubble during the emulgeling process.

The following is the rationale for using emulgel as a system for topical medication delivery Many topical agents, such as ointment, cream, and lotion, have a number of disadvantages. They are extremely sticky when applied, causing discomfort in the patient. They also have a lower spreading coefficient and require rubbing to apply. They also have an issue with consistency. As a result of all of these factors, With in the principal group of semisolid preparations, the usage of translucent gels in cosmetics and pharmaceutical preparations has expanded. Surface tension between a 99 percent weight liquid colloid and a macromolecular network of fibres made from a small amount of gelatin substance present immobilises a gel. Despite the numerous advantages of gels, one significant disadvantage is the delivery of hydrophobic drugs. An emulsion-based approach is being used to successfully incorporate and deliver even a hydrophobic therapeutic moiety through gels to overcome this limitation [7].

Medicated products are applied to the skin or mucous membrane to improve or restore a fundamental function of the skin or to alter the pharmacological action of the underlined tissues. These items are referred to as topical or dermatological products. Many topical agents, such as ointments, creams, and lotions, have several disadvantages. They are sticky by nature, causing discomfort to the patient when applied, and have a low spreading coefficient, necessitating rubbing application. They also have a problem with stability.

Drug absorption through the skin is influenced by a number of factors [8, 9].

Physiological factors

1. The skin's thickness is the first factor to consider.
2. The presence of lipids is number two.
3. The total number of hair follicles in a particular area.
4. The body's total number of sweat glands.
5. Your skin's pH level.
6. Circulation of blood.
7. Inflammation of the skin.
8. Hydration of the skin.

Physics and chemistry factors

1. The partition coefficient.
2. The mass of a molecule (approximately 400 Dalton).
3. The degree of ionisation (only unionised drugs gets absorbed well).
4. Automobiles have a significant impact on the environment.

Physiology of the skin [10, 11]

The majority of topical medications are designed to be applied to the skin.

As a result, a fundamental understanding of the physiology and function of the skin is required. The average person's skin has a surface area of about 2m2, which is important in the development of topical dosage forms.

A third of the blood in the body circulates through the epidermis, which is not alive. On average, bacteria are found on 40% of the surface of the human skin. There are 70 hair follicles and 200-300 sweat ducts in each square. a tenth of a centimetre of skin The pH of the skin ranges from 4 to 5.6. The pH of the skin's surface is affected by sweat and sebum-secreted fatty acids. The skin is made up of four distinct layers of tissue.

Epidermis that is no longer viable

The stratum corneum is the skin's outermost layer, and it acts as a physical barrier to most substances. The stratum corneum is 10 to 20 cell layers thick over the majority of the body. Each cell is a flat, plate-like structure with a surface area of 750 to 1200 m that is brick-like stacked on top of each other and measures 34-44 m long, 25-36 m

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wide, 0.5 to 0.20 m thick, and 0.5 to 0.20 m thick. The stratum corneum is composed of lipid (5-15%), which includes phospholipids, glycosphingolipids, cholesterol sulphate, and a neutral lipid, and protein (75-85%), which is mostly keratin.

The epidermis that is still alive

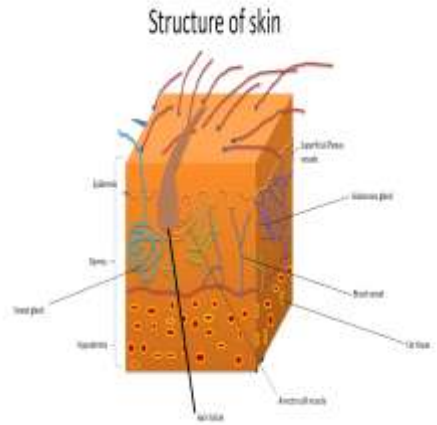
This is a 50-100 micrometre thick layer of skin that lies between the stratum corneum and the dermis. The cells of the viable epidermis have structures that are similar to those of other living tissues in terms of physicochemical properties. The glue that holds cells together is called tono fibrils. This region has a density similar to that of water. Water makes up about 90% of the total weight.

Dermis

Underneath the viable epidermis is the dermis. It's a structural fibrin, and histologically, only a few cells that look like it can be found in normal tissue. The dermis is a loose connective tissue matrix made up of fibrous protein embedded in an amphorphose ground substance that has a thickness of 2000 to 3000 m.

Connective tissue beneath the skin

The hypodermis, or subcutaneous tissue, is not considered a true part of the structured connective tissue, which is made up of loosely textured, white, fibrous connective tissue with blood and lymph vessels, sweat gland secretary pores, and cutaneous nerves. The majority of researchers believe the drug enters the circulatory system through the skin before reaching the hypodermis, though fatty tissue may act as a barrier.



(fig1)

There are a few things to consider when choosing a topical preparation.

[12, 13, 14]

1. The effect of the vehicle, such as an occlusive vehicle, on the active ingredient's penetration and efficacy. It is possible for the vehicle to have its own cooling, drying, emollient, or protective properties.
2. Determine which preparation is best for the lesions. Avoid greasy ointments if you have acute weepy dermatitis, for example.
3. Select a preparation method that is appropriate for the environment. (A gel or lotion, for example, for hairy areas)
4. Irritation or sensitization potential Gels are generally more irritating than ointments and w/o creams. Ointments aren't for you if you're allergic to preservatives or emulsifiers.

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Drugs are delivered through the skin

The epidermis and dermis are two of the skin's most important layers. Blood vessels are densely packed in the skin's subcutaneous layer. The three main mechanisms for drug absorption through the skin are intercellular, transcellular, and follicular drug absorption. The pilosebaceous route is the next most popular delivery method. The intercellular matrix is usually used for permeation, but it has been shown that the transcellular pathway can provide a faster alternative for highly polar molecules. When the skin is healthy and well-preserved, The horny layer's keratinized corneocytes and largely non-polar lipid intercellular cement have been identified as major factors in maintaining an effective drug barrier [15]. Organic solvents like propylene glycol, surfactants, and DMSO can help with skin drug penetration. Permeation enhancers alter the stratum corneum's barrier properties through a variety of mechanisms, including increasing solubility, partitioning the stratum corneum, and fluidizing the crystalline structure of the stratum corneum [16]. Medicated creams and gels applied to the skin have been used to treat infections and pain for many years. Thanks to new technologies, other drugs can now be absorbed through the skin. These can be used to treat the entire body, not just the affected skin.

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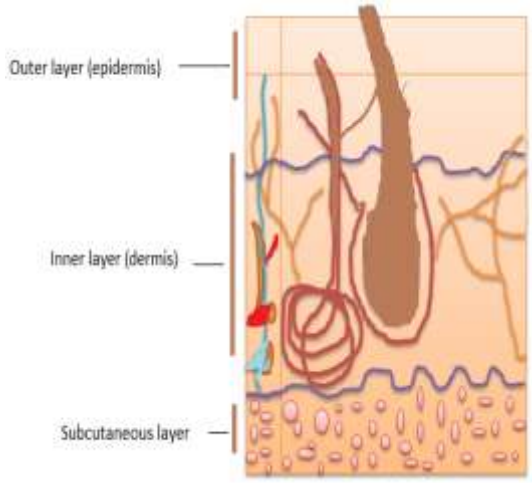

fig 2

Emulgel preparation

This is an aqueous substance that forms the emulsion's aqueous phase. Agents such as water and alcohol are frequently used [17].

Oils

The oily phase of the emulsion is caused by these agents. Mineral oils are widely used as the drug's vehicle as well as for their occlusive and sensory properties in externally applied emulsions, either alone or in combination with soft or hard paraffin. Non-biodegradable mineral and castor oils, which have a local laxative effect, as well as fish liver oils or various fixed vegetable oils (e.g., Arachis, cottonseed, and maize oils) are commonly used in oral preparations as nutritional supplements [18,19].

Table1 (use of oil)

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

Emulsifier

Emulsifiers are used to control and stabilise the emulsification process. Emulsions can be made more stable by incorporating an appropriate emulsifying agent because they are thermodynamically unstable. O/w emulsions are made with surfactants with HLB values greater than 8, such as nonionic surfactants (spans, tweens), whereas water in oil emulsions are made with mineral oils with HLB values less than 8, such as liquid paraffin. When compared to the individual systems of span or tween, mixtures of span 20 and tween 20 result in greater emulsion stability. [20]

Enhancers of permeation

These are substances that temporarily thin the skin's impermeability to aid in the absorption of penetrant through the skin.

Gelling Agents: Gelling agents are used to combine emulsion and water to make a gel base. To make an emulgel, you'll need a gel formulation. These are thickening agents that swell in the aqueous phase and form a gel-like structure, increasing the consistency of any dosage form. [21] A system becomes thixotropic when a gelling agent is added to it. [22] In terms of drug release rate, HPMC-based Emulgel outperformed Carbopol-based Emulgel. Emulgels based on NaCMC were chosen for vaginal use because they had a higher mucoadhesivity, which increased drug residence time and gave the best in-vitro and in-vivo results. HEC-based emulgels had low mucoadhesion but excellent drug release profiles and rheological properties.

Table 2 **VARIOSUS GELLING AGENTS USED IN PHARMACEUTICAL DOSAGE FORMS**

S.No	Gelling agent	Concentration Used % (W/W)	Pharmaceutical Adaptability	Active Pharmaceutical ingredient	References
1.	Carbopol-940	1%	Because of the high viscosity of the gel,	Mefenmic acid	23

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			ensure that the API is released in a controlled manner.		
2.	HPMC	2.5%	Having a high level of stability, as well as microbiological resistance	Clorphenesin	24
3.	Sodium CMC	3-4%	As a result, stand autoclaving is appropriate for sterile gels.	Benzydamine	25
4.	Pemulen	0.1-0.4	Provide quick oil phase release and high stability.	Flubiprofen	26
5.	Combination of HPMC & Carbopol	1.2%	Combination improve stability	Ketorolac, clotrimazole	27
6.	Pluronic®F127	1-3%	cold water, it has improved clarity and solubility.	Piroxicam	28
7.	Carbopol-934	1%	Allow for a controlled release of APIs that have been included.	ChlorPhenesin	29

Formulation of emulgel [30-31]:
Step 1: Prepare the gel with the gelling agent: Weighing a sufficient amount of Carbopol 940 (1 percent w/w) and continuously stirring it into warm distilled water The dispersion was allowed to hydrate for 1-2 hours.
After that, other ingredients like propylene glycol (10% w/w) and glycerol (10% w/w) were added to the aqueous dispersion with constant stirring.
A required amount of drug (1% w/w) was added and evenly dispersed. The dispersion was neutralised to pH 6 with triethanolamine, and the final weight was adjusted with distilled water. The gel was sonicated for 15 minutes and then left overnight to remove air bubbles.
Step 2: Emulsion Preparation: Emulsion preparation varies depending on whether the emulsion is an oil in water or a water in oil.
Step 3: Emulsion incorporation into gel base: To create emulgel, the emulsion was finally incorporated into the gel base.

4. **Characteristics of Emulgel:**
4.1 Physical appearance: The prepared emulgel's colour, homogeneity, and consistency are all checked.
[32]
The pH of the prepared gels' 1 percent aqueous solutions was determined using a digital pH metre. After completely immersing the electrodes in the semisolid formulations, the pH was determined. [33]
Spreadability: To investigate the spreadability of formulations, a special apparatus was developed. The ability of a product to spread over time is referred to as "spreadability."
formulations that sit between and beneath the application
The time it takes to lift a specific load is cut in half. Because the two slides are separated, the spreadability is improved. Two glass slides were chosen, each measuring 6x2 cm. A formulation was applied to one of the slides. Whose spreadability had to be evaluated? (500mg). This slide was layered on top of the previous one in such a way that the formulation was sandwiched between the two slides. The excess of the formulation adhering to the slides was scraped off after the weight was removed. The lower slide was attached to the apparatus's surface, and the upper slide to a string.
Spreadaibility = (M/T)*L
Where, M= Weight which is tied to the upper slide (20gm)
L= Length taken of glass slide (6cm)
T= Time taken (seconds)
The delivery of the correct dose of the drug
Depends highly on the spreadability of the formulation [34].

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Swelling Index: For the purpose of determining the swelling index of formulated emulgels, 1 gm of the gel is placed on porous aluminium foil and then placed separately in a 50 ml beaker containing 10 ml 0.1 N NaOH.

After that, samples were taken from beakers at various time points and placed in a dry place for a while before being reweighed. The following formula is used to calculate the swelling index:

Swelling index= (sw%) = [wt-w0] / w0×100

Where,

Wo denotes the emulgel's initial weight at zero time.

Wt = Swollen Emulgel Weight after Time t (SW) present = Percent Swelling Index [40]

Extrudability of topical emulgels (Tube Test): In this typical experimental test, the force required to expel the material from the tube is measured. Clean, lacquered aluminium collapsible metal tubes were filled with the extrudable formulation. The tubes were pressed with a finger to extrude the material. The quantity in percentage of emulgel was used to evaluate emulgel formulations for extrudability in this study. The weight in grammes required to extrude a 0.5 cm emulgel ribbon in 10 seconds was used to extrude emulgel from a lacquered aluminium collapsible tube. [41] The experiment was carried out three times (n=3), with the average of the results for each formulation being calculated:

Measurement of bioadhesion strength: The bioadhesion strength was determined using a modified balance method. The two pans' physical balance was thrown off. On the left side, a glass slide was hung, and the right side pan was replaced with a 100 ml beaker. A 20 g weight was hung on the left side of the assembly to balance it. Underneath the first glass slide, a second was hung. Both slides had hairless fresh rat skin attached to them. One gramme of gel was placed between two rat skin faces. After applying some pressure to form a bioadhesion bond, water was slowly added to the right side beaker until the gel was separated from the rat skin attached to one face. [35].

To determine the drug content of the gel formulation (1 gramme), it was dissolved in a suitable solvent. I filtered it to get a clear solution. The solution absorbance was measured using a UV Visible spectrophotometer. Using the drug calibration curve [36], the drug content was calculated.

Emulgel in vitro drug release studies were carried out on Diffusion cells using egg membrane. This was carefully clamped to one end of the hollow glass tube of the dial y sis cell. Emulgel (1 g) was applied to the surface of the egg membrane dialysis membrane. The receptor chamber was filled with freshly prepared PBS (pH 7.4) solution to solubilize the drug. The receptor chamber was stirred with a magnetic stirrer. The samples (1 ml aliquots) were collected at appropriate time intervals after appropriate dilutions and analysed for drug content using a UV-visible spectrophotometer. Cumulative corrections were used to determine the total amount of drug released at each time interval. [37]

Ex-vivo skin permeation and retention studies:

We used a 200-250 g albino rat that was 10-12 weeks old. After the excised skin was placed in aluminium foil, the dermal side of the skin was delicately teased off for any subsequent fat and/or subcutaneous tissue. The skin was then meticulously examined with a magnifying glass to ensure that there were no surface irregularities in the part used for transdermal permeation studies, such as small openings or cervices. All of the experiments used skin that had been freshly obtained and washed in physiological buffer saline. The ex-vivo skin permeation of drugs from various formulations was investigated using the Keshary-chien cell.

The effective permeation area of the diffusion cell was 9.8 cm2. The receptor compartment has a volume of 37.5 ml. The epidermis site was in the donor compartment, and albino rat skin was sandwiched securely between the donor and receptor compartments. With constant stirring, the donor compartment was kept at 371 degrees Fahrenheit. The emulgel formulation was applied to the epidermal surface of the rat skin. To ensure sink condition, 3.0 ml of aliquots were removed and replaced with an equal volume of fresh receptor compartment solvent at predetermined time

intervals for 24 hours (0.5hr, 1hr, 2hr, 4hr, 6hr, 8hr, and 24hr). The cumulative percentage of drug diffused across the skin was calculated at each sampling point [38].

Stability Studies: The optimised emulgel formulation was chosen for the stability study. At 5°C, 25°C/60 percent RH, 30°C/65 percent RH, and 40°C/75 percent RH, a sufficient amount of emulgel formulation was sealed in a 10 gm collapsible tube in triplicate and subjected to stability studies for three months. At predetermined time intervals, the samples were tested for pH, physical appearance, rheological properties, and drug content [39].

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Data from ex-vivo permeation studies were fitted into zero order, first order, Higuchi, and mathematical models for the evaluation of drug release kinetics. The best fit model was predicted using the R2 value. The model with the highest R2 value, i.e. the best fit, was the best fit.

TABLE:3 CURRENT ELEVATIONS IN DEVELOPMENT OF EMULGEL FOR VARIOUS DRUGS

Drug	Aim	Uses	References
Acyclovir and Ketoconazole	Acyclovir and ketoconazole are delivered topically.	Cutaneous symptoms of viral and fungal infections	40
Diclofenac Sodium	A comparative bioavailability investigation of diclofenac skin penetration from anovel topical non aqueous solution	Pain relief	41
Diclofenac Sodium	Diclofenac diethylamine nanoemilsion-based gel formulation: design gel, optimization, rheological behaviour, and vitro diffusion investigations	Management of Pain	42
Pinhao stach	New natural cosmetic ingredients: pinaho starch and coat extract: Stability of topical formulations and sensory evaluation	Antioxidant activity	43
Meloxicam	Meloxicam-loaded emulgel formulation and characterization for topical application	Anti-inflammatory	44
Ketoprofen	Formulation, in vitro and in vivo evaluation of a ketoprofen-loaded microemulsion-based gel	Anti-inflammatory	45
Calcipotriol	Calciferol is delivered as an emulgel into the skin for efficient penetration.	In the case of psoriasis,	46
Ketorolac Tromethamine	The use of a noisome–emulgel combination to increase the transdermal permeability of a water medicine	Anti-inflammatory	47
Terbinafine hydrochloride	Terbinafine hydrochloride emulgel formulation and in	In treatment of fungal infection	48
Carboxymethyl beta-glucan Dimethicone,		For treatment of acute and	49

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glycerine, prunusamygdalus dulcis oil, borago officianils seed oil	vitro assessment for topical fungal infection	chronic anal fissure	
Malva sylvestris extract, calendula officinalis extract, glycyrrhiza glabra extract	LEVORAG® Emulgel's safety and efficacy in the treatment of acute and chronic anal fissures in a prospective multicenter observational trial	Topical ocular delivery	50
Cyclosporin A	Cyclosporin formulation and testing An ocular delivery emulgel	Hypoxic cell radiosenstizing agent	51
Nimorazole			52
Allopurinol		In treatment of Psoriasis.	53
Silver Sulfadiazine	Nimorazole, a radiosensitizing drug, was prepared and evaluated in a topical emulgel.	Antimicrobial activity	54
Terpinen-4-ol	Allopurinol emulgel design and development Silver sulfadiazine emulgel development and characterisation for topical medication delivery	Antimicrobial properties	55
Betamethasone dipropionate	Terpinen-4-ol released and permeation profiles as a function of emulgel rheological behaviour and microstructure	For the treatment of atopic dermatitis	56
LEVORAG® Emulgel :Hibiscus esculents extract,		Leishmaniasis Therapy	57
Amphotericin B	The creation of a betamethasone dipropionate-loaded nanostructured lipid carrier for use as a topical ointment	Passive and iontophoretic delivery of therapeutics	58
Metronidazole and ciprofloxacin			59
Amlodipine besylate	Evaluation of amphotericin B emulgel's in vivo 1eishmanicidal activity: An alternative for the treatment of cutaneous 1eishmaniasis	Transdermal delivery Viral and fungal cutaneous manifestations	60
Acyclovir and Ketoconazole	Emulsion gels based on ground nut oil for passive and iontophoretic medicinal delivery	Antihypertensive	61

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Lacidipine	Preparation and percutaneous permeability of amlodipine besylate emulgels for transdermal delivery in vitro Acyclovir and ketoconazole are delivered topically.	Anti-inflammatory	62
Piroxicam Pravastatin	Novel non-ionic surfactant proniosomes for lacidipine transdermal delivery: optimization with a 23 factorial design and in vivo testing in rabbits	Pain relief	63
	Percutaneous absorption of piroxicam from emulgels with various penetration enhancers		
	An Insight into the Thermal, Mechanical, and Electrical Studies of Optimised Transdermal Delivery of Pravastatin Genipin-Crosslinked Gelatin-Based Emulgels		

Various Emulgel formulations that are commercially accessible: Emulgel is commercially available in markets, with certain preparations indicated in Table. Voltaren Emulgel is a topical analgesic gel that improves shoulder and back pain by reducing swelling. Voltaren Emulgel is a non-greasy, pleasant-smelling gel that comes in a 100g tube and contains diclofenac sodium 1 percent w/w as the active ingredient (as diclofenac). diethylamine). Torrent Pharma's Diclomax Emulgel is another emulgel for treating inflammation of the tendons, ligaments, muscles, and joints. Miconaz H emulgel contains the active chemicals miconazole nitrate and hydrocortisone, which have bactericidal, fungicidal, anti-inflammatory, and antipruriginous effects. Medical Union Pharmaceuticals is the company that makes it.

Table 4VARIOUS MARKETED EMULGEL FORMULATION

Marketed formulation	**API**	**Manufacture**	**Use**
Diclomax Emulgel	Diclofenac sodium	Torentpharm	Anti- inflammatory
Voltarol 1.16% Emulgel	Diclofenacsodium	Novartis	Anti -inflammatory
Miconaz-H-emulgel	Miconazole nitrate, Hydrocortisone	Medical union Pharmaceuticals	Topical Corticosteroid and anti-fungal

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II. CONCLUSSION:

Emulgel is a new way to distribute hydrophobic medications topically that combines the benefits of emulsion and gel to improve patient acceptance. Emulgel aids in the spreadability, adhesion, viscosity, and extrusion of liquids. It has uses in pharmaceutical and cosmetics, as well as the ability to include herbal compositions.

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