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A REVIEW ON ALOE VERA EMULGEL FOR TOPICAL APPROACH

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ABSTRACT

Cosmetics are designed to be applied to the skin, and it is a common approach for local and systemic treatment. As cosmetics, these days are mixed with a variety of chemicals causing more side effects; people prefer the products derived from a plant source as they are less harmful to the skin, and such products are called "Herbal cosmetics" and one such product is "*Aloe Vera*."*Aloe Vera*gel in its raw form hastens the healing of burn wounds. So, *Aloe Vera*can be given by topical delivery; it can go through deeper layers of the skin and provide greater absorption. For hydrophobic drug, Emulgels must be employed as a topical drug delivery mechanism. Emulgel is a combination of emulsion and gel.*Aloe Vera*was extracted and used as a gel and emulsion is incorporated into it, becomes a dual-control release system, as well as more stable. Emulgel has bio-friendly, thixotropic, readily spreadable, greaseless, and readily removable, water soluble, skin softness, transparency, and non-staining, pleasing appearance. This article provides an overview of the optimal features, production, and characterisation of Emulgels in order to better comprehend their potential as delivery vehicles. The application of Emulgel-based systems as drug delivery vehicles is examined, with a focus on current developments and future directions.

INTRODUCTION

Nowadays, people of all ages utilise cosmetic goods, which has resulted in fewer skin issues ranging from hyper-pigmentation to skin ageing. The term "kosmetics" refers to the act of adorning (more attracting). Cosmetics are a type of health and beauty product that alters a person's look. These are meant for topical use. They include a variety of goods that are used to care for the skin and add scent to the body. It is made up of a variety of chemical components that have been produced from natural or synthetic sources. People prefer products that are totally derived from an original plant source since they are less toxic to the skin; such products are referred to as "herbal cosmetics," and one such product is "*Aloe Vera.*" The botanical name of *Aloe Vera* is Aloe barbadensis miller. Aloe was earlier considered to belong to family Liliaceae, but at present it is placed in the family Aloaceae. [1] It's a perennial, succulent plant with a shrubby appearance. The leaves of the Aloe plant have a high amount of water retention, allowing the plant to survive extreme conditions such as long periods of drought and a hot, dry climate.

Aloe Vera is said to have 75 nutrients and 200 active substances, including enzymes, amino acids, minerals, vitamins, anthraquinones, saponins, lignin, and salicylic acid. [2] The Aloe gel contains 96% of water and the rest 4% of vitamins A, B, C, E, calcium, enzymes and amino acids. The leaf's inner section creates a thin, transparent, tasteless jelly-like substance. The *Aloe Vera* gel is popular because of its anti-inflammatory, antidiabetic, antioxidant, immune boost, anticancer and anti-ageing propertiesdespite the use of a variety of modern skin care products and treatments, *Aloe Vera* gel in its raw form hastens the healing of burn wounds. Mannose-6-phosphate, a component of *Aloe Vera* that stimulates the proliferation and migration of fibroblasts and keratinocytes and may have a role in wound healing, is made up of linear chains of glucose and mannose molecules by topical delivery. [3]

So, *Aloe Vera* can be given by topical delivery; it can go through deeper layers of the skin and provide greater absorption. [4] Topical drug administration is a localised drug delivery system that can be used to administer drugs to any part of the body via ophthalmic, rectal, vaginal, and cutaneous channels. This approach is considered as an effective treatment especially for fungal infections. [5] Most of the pharmaceutical formulations which are meant to apply onto the skin are prepared in such a way to provide extended local contact with least systemic drug absorption. [6] Topical drug delivery avoids first pass metabolism and enhances bioavailability of the formulation preparation.

The topical drug approach also includes the use of semisolid dosage forms like creams, ointments and lotions but they are bulkier and they have less spreading coefficient hence they

are rubbed onto the skin and they also display the problems of stability and duration of action [7] So as to overcome all these problems, the use of transparent gels benefits a lot for example. presence of the high liquid content in the gel feels very light on the skin and does not make it greasy or clog pores thus bringing out convenience to the victim up on administration. Gels are made by trapping large volumes of aqueous (or) hydroalcoholic liquids in a network of colloidal solid particles such as polymers, which can be either natural or manmade. [8] Gels has more appreciable properties like easy to formulate and exhibit appreciable properties like prolonged action, good adherence property to the site of application, biocompatible and eco-friendly and have magnificent tolerability to stress conditions. [9]Even though there are many benefits of gel a major restriction is in the delivery of hydrophobic drugs. To improve drug distribution, multiple formulations are sometimes blended; emulgel is a best form.

Emulgel is an advanced approach for effective delivery of a drug, depending on combined approaches i.e., is a mixture of emulsion and gel. [10] Emulgel is formulated both in oil-in-water type and water-in-oil type emulsion and then entrapped into a gel. In this, oil-in-water type is used for delivery of lipophilic drugs whereas; water-in-oil type is used for delivery of hydrophobic drug. [11] The emulsifying agent, gelling agent, and oil phase are the three main components of emulgel. [12]The application of a gelling ingredient can transform a traditional emulsion into an emulgel.[6]Therefore, enhancing stability, drug loading capacity and providing long duration of action.Emulgel has bio-friendly, thixotropic, readily spreadable, greaseless, and readily removable, water soluble, skin softness, transparency, non-staining, pleasing appearance. [13] Emulgel is now being employed as a carrier for delivery of the drug to the skin. [14] Because the emulgel preparation is intended to be administer through the skin, a fundamental understanding of skin physiology and drug penetration across skin is essential for creating emulgels.

PHYSIOLOGY OF SKIN[22-23]

The majority of topical medicines are intended for use on the skin. As a result, a fundamental understanding of the skin's physiology and function is critical for developing topical dose forms. A typical adult's skin has a surface area of around 2 m^2 and receives around one-third of the blood that circulates throughout the body. On the average, every square centimetre of human skin has 40–70 hair follicles and 200–300 sweat ducts. The skin's pH ranges from 4 to 5.6. Sweat and sebum-secreted fatty acids affect the pH of the skin's surface. There are four separate layers of tissue that make up the skin.

REVIEW OF LITERATURE

S. No	Drug	Inference	Reference
1.	Terramycin	Authors formulated and evaluated *Aloe Vera* hydro gel containing antibiotic. They reported that prepared formulation exhibits activity in less than 5 days where as aloe vera gel exhibits activity in 10 days.	[15]
2.	*Aloe Vera*	Authors formulated and evaluated *Aloe Vera* emulgel for topical application using carbomer. They reported that aloe vera extract can be used for application on to skin.	[16]
3.	Desoximetasone (DMS)	Authors formulated and evaluated aloe vera mediated emulgel. They reported that the prepared formulation is effective against plaque psoriasis.	[17]
4.	*Aloe Vera*	Authors formulated and evaluated *Aloe Vera* tooth gel. They reported that the prepared formulation has shown lesser side effects when compared to synthetic formulation.	[18]
5.	*Aloe Vera*	Authors reported topical application of *Aloe Vera* has enhanced morphological, biochemical, and biomechanical properties of the healing cutaneous wounds in rats.	[19]
6.	*Aloe Vera*	Authors formulated and evaluated *Aloe Vera* tooth gel with active salt. They reported that the prepared formulation is competent of diminishing the plague, bad odour.	[20]
7.	*Aloe Vera*	Authors formulated and evaluated *Aloe Vera* hydrogel. They reported that the prepared formulation exhibited good physico chemical properties.	[21]

Non-Viable Epidermis

The stratum corneum is the skin's the topmost layer, and it serves as a physical barrier to most substances that come into touch with it. Over the majority of the body, the stratum corneum is 10–20 cell layers thick. Each cell is a plate-like structure with a flat surface that is 34–44 metres long, 25–36 metres wide, and 0.5–0.20 metres thick, with a surface area of 750–1200 metres, arranged in a brick-like manner. The stratum corneum is made up of phospholipids, glycosphingolipids, cholesterol sulphate, and a neutral lipid (5–15%), as well as protein (75–85%), which is primarily keratin.

Viable Epidermis

Between the stratum corneum and the dermis, this layer of the skin has a thickness of 50 to 100 micrometres. The cells of the live epidermis have structures that are physiochemically comparable to those of other live tissues. Tonofibrils are the glue that holds cells together. The density of this area is similar to that of water. The water content is approximately 90%.

Dermis

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

Subcutaneous Connective Tissue

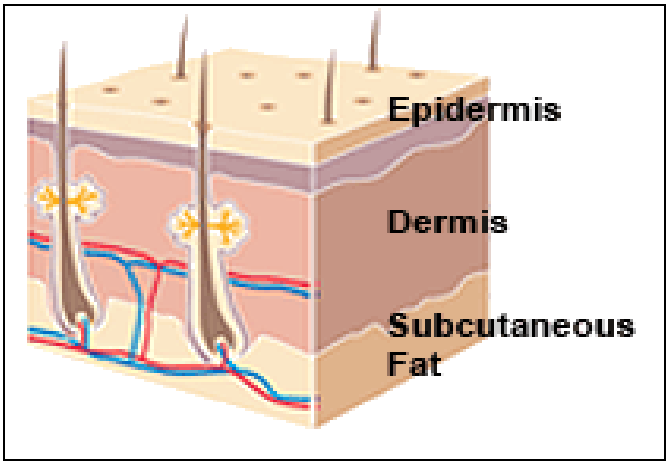

Fig.1:Layers of Skin

(American Academy of Dermatology)

The hypodermis, or subcutaneous tissue, is not regarded a real part of the structured connective tissue, which is made up of loosely textured, white, fibrous connective tissue that contains blood and lymph arteries, sweat gland secretary pores, and cutaneous nerves. Most experts assume that the medication enters the circulatory system through the skin before reaching the hypodermis, and that the fatty tissue serves as a storage site for the medication. [24]

Drug penetration through skin

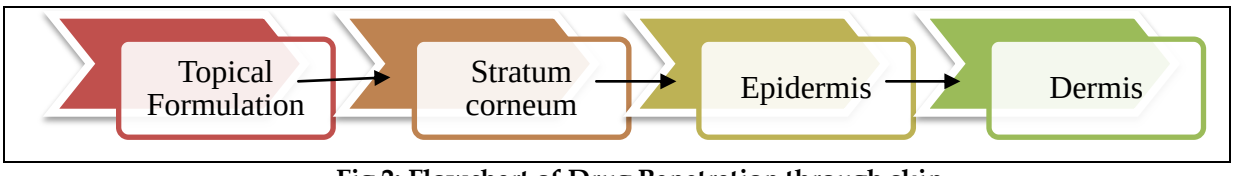

Fig.2: Flowchart of Drug Penetration through skin

The epidermis is the skin's most superficial layer, made up of stratified keratinised squamous epithelium that varies in thickness across the body. The epidermis and dermis are the two most significant layers of the skin. The subcutaneous layer of the skin is densely packed with blood vessels. Intercellular, transcellular, and follicular drug absorption are the three main pathways for drug absorption via the skin. The pilosebaceous route is the second most prevalent mode of distribution. Permeation usually occurs through the intercellular matrix, although it has been demonstrated that the transcellular channel provides a quicker alternative route for highly polar compounds. The keratinized corneocytes and the predominantly non-polar lipid intercellular cement of the horny layer are the principal components involved in the maintenance of an effective drug barrier in normal undamaged skin. The barrier qualities of the stratum corneum are affected by permeation enhancers through a variety of mechanisms, including increasing solubility, partitioning the stratum corneum, and fluidizing the stratum corneum's crystalline structure. [25] Medicated creams and gels administered to the skin are used to treat infections & discomfort for many years. Other drugs could now be absorbed through the skin. Through a systemic approach, these can be used to heal not just the injured skin regions, but the entire body.

RATIONALE OF EMULGEL AS TOPICAL APPROACH

Cosmetics are made up of a wide range of chemical components derived from both natural and manmade sources. People prefer products that are entirely derived from a natural plant source since they are less toxic to the skin; such products are known as "herbal cosmetics," and "*Aloe Vera*" is one of them. So, *Aloe Vera*can be given by topical delivery. Topical drug delivery avoids first pass metabolism and enhances bioavailability of the formulation. To create a topical formulation that incorporates a hydrophobic drug that is not conceivable with a simple hydrogel, and can only be done with Emulgel (emulsion+ gel).[16] Many commonly used topical treatments, such as ointments, creams, and lotions, have numerous drawbacks when it comes to improving patient compliance. When administered, they are extremely sticky, creating discomfort in the sufferer. Furthermore, they have a lower spreading coefficient and must be rubbed on, and they have a problem with stability.[26] The usage of transparent gels in cosmetics and medicinal preparations has increased as a result of all of these variables inside the main category of semisolid preparations. Despite the many benefits of gels, one important drawback is the delivery of hydrophobic medicines.

APPLICATIONS

Aloe Vera is used to make a range of goods, including juice, concentrate, and powder. The next sections go through some of its uses in medications, foods, and cosmetics.

1. Healing Wounds

Wound healing is the process of recovering the viability of injury site. *Aloe Vera* contains amino acids that are important in the wound healing process. It induces the production of antibodies in the body and by generating growth factors, it kickstarts wound healing.

2. Anti-Inflammatory

Because anthraquinones are present in Aloe gel, it has potent anti-inflammatory properties. Oral Aloe gel (2%) has been shown to help individuals with aphthous stomatitis reduce the level of their discomfort and the size of their wound.[27] *Aloe Vera's* anti-inflammatory properties aid in the relief of joint discomfort.

3. Anti-Cancer Activity

*Aloe Vera*contains glycoproteins and polysaccharides that make it a powerful chemopreventive agent that can be used to treat a variety of malignancies. These substances boost the immune system's ability to fight cancer.

4. Antidiabetic Activity

In the treatment of type 2 diabetes, Aloe gel is an efficient antihyperglycemic medication. It reduces blood glucose levels while maintaining normal blood lipid levels and liver/kidney function.[28]

5. Antihyperlipidemic Activity

*Aloe Vera*gel has been shown to have Antihyperlipidemic properties. It successfully lowered blood cholesterol (15.4 percent), triglycerides (25.2 percent), and LDL cholesterol in individuals who were not responding to dietary treatments (18.9 percent).[29]

6. Teeth and Gum Protection

*Aloe Vera*is commonly used in dentistry to treat a range of dental issues, including pain relief and faster recovery following periodontal flap surgery. *Aloe Vera* is used to treat gum illnesses including gingivitis and periodontitis by reducing bleeding, controlling inflammation, and stopping gum swelling. [30]

7. Food Applications

Aloe Vera is used as a nutritional supplement and a usefulelement in a variety of foods.

Aloe gel contains mannose polymers as well as certain carbohydrates such as glucose and ace Mannan. These, in combination with glycoprotein's, enzymes, amino acids, and vitamins, help foods operate without compromising their excellence or adequacy.[31]

8. Cosmetic Application

Aloe Vera gel is broadly utilized in cosmetics business. It's utilized as a basis for a variety of formulations, including moisturizers and sun lotions, and it's also utilizedashumectants in skin preparations. [32]

Because of its important moisturizing and calming benefits inside products like shampoos, soaps, cleansers, and

moisturizingcream. Soaps made with Aloe gel contain the benefit of causing no irritation and leaving the skin moisturized.

BENEFITS OF EMULGEL [26]

1. Hydrophobic drugs can be incorporated.
2. Bypasses First Pass Metabolism.
3. Improved patient compliance.
4. Better Stability.
5. No intense sonication.
6. Prolonged duration of action.
7. More selective for a site specific.
8. More loading capacity.
9. Preparation cost is low.

LIMITATIONS OF EMULGEL [33]

1. Large-particle drugs are difficult to absorb through the skin.
2. Allergic reactions are a possibility.
3. Some medications have a low permeability all the way through the skin.
4. The incidence of a bubble during emulgel formulation.

Various Adjuvants used in Emulgel Preparation

1. **Aqueous Material**

   The aqueous phase is water, alcohol.[34]

2. **Oils**

   The oily phase of the emulsion is formed by mineral oils, either alone or in combination with soft or hard paraffin's, are commonly employed as the drug's carrier as well as for their occlusive and sensory properties in topically administered emulsions.[36]

3. **Emulsifiers**

   Emulsifying chemicals are used to enhance emulsification during the manufacturing process as well as to maintain stability during a shelf life that can range from days to months or years for commercial preparations. Polyethylene glycol 4031 stearate, Sorbitan monooleate32 (Span 80), Polyoxyethylene Sorbitan monooleate (Tween 80)33, Stearic acid34, Sodium stearate35 are some examples.[26]

4. **Gelling Agents**

   These are thickening agents that are used to enhance the consistency of any dose form Examples include carbopol-934, HPMC etc.

5. **Permeation Enhancers**

   These are substances that partition into skin components and interact with them to cause a transient and reversible increase in skin permeability. Examples include clove oil, oleic acid etc. [36]

***Aloe Vera* Extract preparation**

A few Aloe leaves were gathered from an Aloe barbadensis Miller plant and were cleaned properly with water. The yellow layer just underneath the green rind was gently scraped off with a sharp knife, avoiding the vascular bundles, and then the top rind was removed. The bottom rind was also removed to get rid of the substantial amount of mucilage that clings to it. A spoon was used to scoop up the transparent mucilaginous gel. The plant extract was filtered through a Whattman filter paper

after 50 mL of crude clear *Aloe Vera* extract was blended uniformly using a magnetic stirrer. It was then put into a, clean glass jar and kept in the refrigerator. [3]

Gel Base Preparation

The gel base was made by dispersing 1% carbomer 940 in distilled water at 80°C, swirling constantly at a moderate speed with a magnetic stirrer, and adjusting the pH to 6-7 with triethanolamine (TEA). It was then infused with 50 mL of *Aloe Vera* extract, and a gel base based on *Aloe Vera* extract was created.[37]

Emulsion Preparation

Span 20 was dissolved in light liquid paraffin to make the oil phase of the emulsion, while Tween 20 was dissolved in filtered water to make the aqueous phase. Methyl and Propyl paraben were dissolved in propylene glycol, while the drug was dissolved in ethanol, and both solutions were combined with the aqueous phase. Both the oily and aqueous phases were heated to 70° to 80°C separately, then the oily phase was added to the aqueous phase and stirred continuously until the mixture reached room temperature. [37]

***Aloe Vera* Emulgel Preparation**

To make the Emulgel, Glutaraldehyde was added to the prepared *Aloe Vera* gel and emulsion mixture in a 1:1 ratio throughout the mixing process.

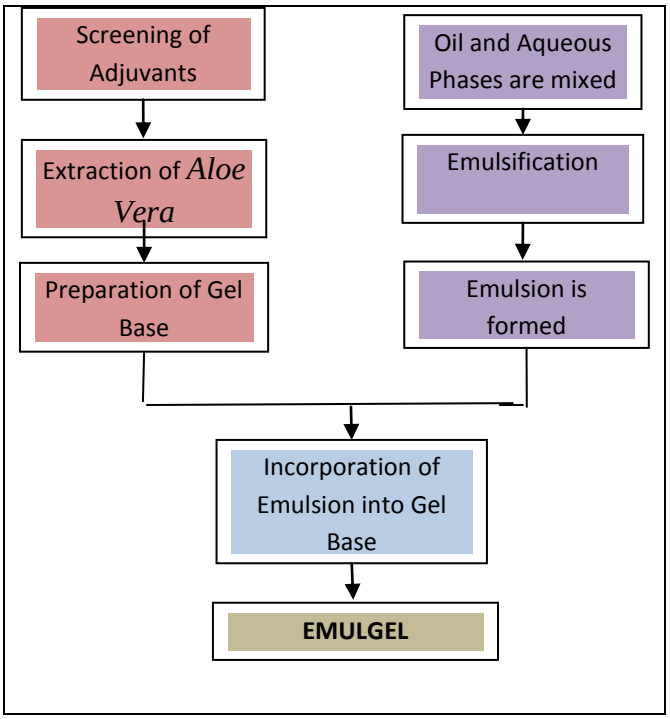

Fig.3: Preparation of Aloe Vera Emulgel

Evaluation Parameters

Physical Examination:

Color, homogeneity, consistency, and phase separation are all examined in this step. [38]

1. **Spreadability:**

A specific apparatus was created to investigate the spreadability of formulations. Spreadability is measured by the time it takes two slides to separate from formulations placed between them in seconds. The shorter the time it takes for the two slides to separate, the greater the spreadability.

2. **pH:**

A digital pH metre was used to determine the pH of the produced gels. The pH of the semisolid formulations was measured after the electrodes were completely dipped in them. [6]

3. **Rheological Study:**

At 25°C, the viscosity of the various emulgel formulations is evaluated using a cone and plate viscometer with spindle 52 (Brookfield Engineering Laboratories) and a thermostatically controlled circulating water bath.[39]

4. ***In-vitro* Drug Release Study:**

It's done with the use of a Franz diffusion cell. It aids in the determination of medication release. [40]

5. **Microbiological Assay:**

The ditch plate technique is employed in this procedure. This approach is used to assess bacteriostatic or fungistatic activity.

6. **Accelerated Stability Studies:**

It is carried out in accordance with ICH recommendations. For three months, the stability test is carried out in a hot air oven at 37±2°C,45±2°Cand60±2°C.

7. **Drug Content:**

A spectrophotometer is used to determine the drug concentration in Emulgel. A known amount of Emulgel is dissolved in a solvent (methanol) and sonicated if necessary. In a UV spectrophotometer, absorbance is measured after a proper dilution.

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

8. **Globule Size and Distribution in Emulgel:**

Malvern Zetasizer is the one which determines size and distribution of Emulgel. To ascertain the value, the emulgel is dissolved in water, stirred, and placed into the device.[41]

9. **Centrifugation Study:**

This procedure is used to determine the emulgel's stability. After a week of preparation, it is completed. The experiment was carried out in a minicentrifuge at 3000 rpm for 30 minutes.

10. **Swelling Index:**

One gram of emulgel is put individually in a 50 ml beaker containing 10 ml of 0.1 N NaOH in a porous aluminium foil. The samples are then withdrawn at various intervals and reweighed. The equation for calculating the swelling index is:

Swelling Index %=[(Wt-Wo)/Wo]×100

Where Wt is the weight of the swelled emulgel at time t, and

Wo is the emulgel's original weight at zero time.

11. Skin Irritation Test:

Because the medication is a topical formulation, this test is critical. The test is done on the skin of the animal. After applying the emulgel to the animals' skin, they are returned to their cages. The animals are evaluated after 24 hours. The emulgel is then washed away from the location using tap water.

12. Stability Studies:

The emulgel was packaged in aluminum collapsible tubes and kept in harsh circumstances before being tested for stability.

MARKETED PRODUCTS

Emulgel as a Topical Approach has many marketed products and are given below:

S.NO	Brand name	Generic name	Company name	Effect
1	Voltaren emulgel	Diclofenac-Diethyl-Ammonium	Novartis Pharma	Anti-inflammatory
2	Pernox gel	Benzoyl Peroxide	Cosme Remedies Ltd.	Anti-bacterial
3	Diclomax emulgel	Diclofenac-diethyl amine	Torrent Pharma	Anti-inflammatory
4	Miconaz-H-emulgel	Miconazole nitrate hydrocortisone.	Medical Union Pharmaceuticals	Anti-fungal
5	Denacine Emulgel	Clindamycin phosphate	Beit jala pharmaceutical company	Anti-acne emulgel

FUTURE SCOPE

*Aloe Vera*is one of the most prominent products. It is used for thousands of years. It is noted as a "Miracle Plant". [42] It has actions of antiseptic, anti-inflammatory, and cure for heat burns to relieve severe illness symptoms like cancer and diabetes to bring a beauty aid and health nourish. It also serves as an alternative medicine for wound healing. So, *Aloe Vera* is basically given by topical approach. Different delivery techniques, such as ointments, lotions, creams, and pastes, are used for topical drug delivery. These topical formulations often comprise a large range of hydrophobic oleaginous bases, such as petrolatum, beeswax, or vegetable oils, which cannot contain water or an aqueous phase. It makes them an excellent emollient, but it also inhibits drug release and thickens and greasy the product.

In comparison to other topical administration systems, gel provides an aqueous environment for the medication, allowing for faster drug release and breakdown. Emulsion-based gels are a good choice for delivering hydrophobic medications to the skin since they can be integrated into the oily phase and administered to the skin. All of these characteristics make emulgel more efficient and productive than alternative topical delivery techniques. These qualities will be exploited in the future to administer a greater variety of topical medications in the form of Emulgels.

CONCLUSION

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. This will become a popular topical drug delivery system.

Conflicts of interest:

No conflict of interest was declared by the authors. The authors alone are responsible for the content and writing of this article.

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