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Evolving Implementation of Emulgel as a Topical Drug Delivery System: A Systematic Review

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ABSTRACT

Emulgels are a new drug delivery technology for hydrophobic drugs that have received popularity in recent years. This formulation is a blend of emulsion and gel, and it is an innovative type of drug delivery mechanism. The goal of this review is to gain insight into emulgel preparation and evaluation to determine how essential these dosage forms are. It will be widely utilized in the future since it is simple to use and improves patient compliance. Emulgels are readily removed, spreadable, thixotropic, greaseless, pleasant, emollient, have a long shelf life, and are clear. Gels have several advantages, but their delivery of hydrophobic agents is one of them. To solve this constraint, an emulsion-based technique is being developed. Emulgel is a unique topical medication delivery technology since it has both a gel and an emulsion release control system. When emulsions are mixed with gel as a form of administration, an emulgel with the dual release is created. Polymers with better release patterns have emerged as a consequence of this method, allowing for a controlled and extended-release.

Key words: Emulgel, gelling agent, polymers, emulsions, herbal emulgel

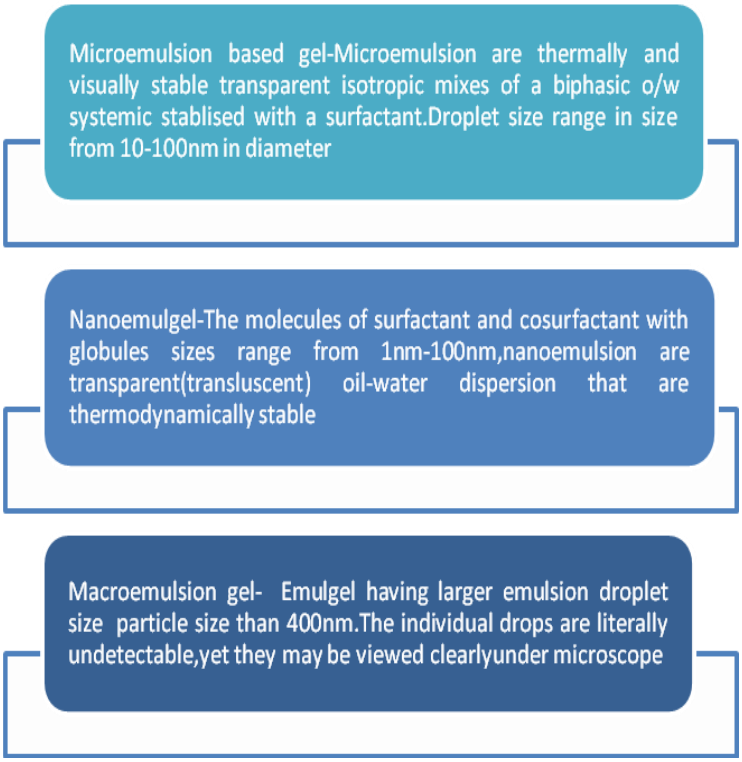
1. INTRODUCTION

One of the most accessible routes for drug distribution in topical drug delivery systems is the skin. For millennia, topical medication distribution has been used to treat dermal illnesses. It is a generalist route of drug administration that may be employed anywhere in the body via ocular, gastrointestinal, genital, and epidermal routes. Academicians and researcher's specialist shave become more interested in pharmaceutical semisolid medication formulations, notably emulgels, throughout the preceding period. The skin is an essential area for the administration of both topical and systemic medications. Even though the skin is a convenient route for medication delivery, some medications do not penetrate the skin. Simple mixture sand lotions to multiform nano medicine therapies are among the topical therapeutic remedies available. Topical medication delivery methods will be employed extensively in the next years to increase patient compliance[1]. Without the need for Bypassing metabolism of starting phase concerns, topical medication administration allows for speedier exposure to the epidermis as a target tissue for treatment and diagnosis.[2]

To disseminate active substances to their target sites, a gel is an advantageous and preferable type of medication. Gel captures tiny drug particles and enables regulated release due to its crosslinked and three-dimensional structure. The presence of a large number of the multi-planar system can store a large number of solvent molecules.[3]

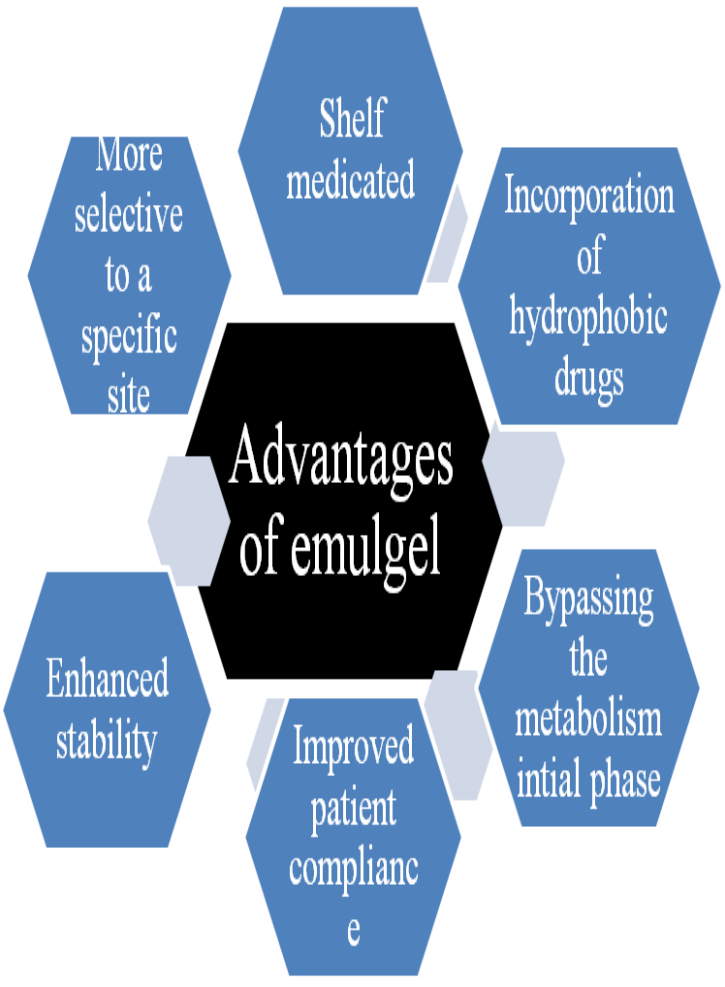
Because of their muco-adhesive properties, gels extend the period that a medicine is in contact with the skin. The majority of pharmaceutical gels are made by dispersing hydrophilic polymers in an aqueous phase. Hydrophilic polymers become lyophilic colloids after dissolving in an aqueous phase. Due to their distinct physical characteristics, they are transformed into conscience suspended particles[4]. Spreading, extrusion, Blemish, and highly viscous properties are all advantages of gels, but when it comes to delivering hydrophobic drugs to the skin, they have a major disadvantage. Because of their lack of solubility in the aqueous phase, hydrophobic active ingredients do not release drugs properly in gels and should not be added to the gel basis. As a result, emulsion-gel based drug delivery techniques are being developed to mitigate these limitations[5]. As a consequence, emulsion-gel based drug delivery techniques are being developed to mitigate these limitations. Emulgel is a formulation in which an emulsion including oil and water is entrapped in a gel phase. Emulgels are any oil-in-water or water-in-oil emulsions that have been gelled by passing through a gelling agent. For, hydrophobic or weakly water-soluble medications, the emulsified gel offers a stable and appropriate carrier. In a nutshell, emulgels are a hybrid of an emulsion and a gel[6,7]. The use of novel polymers that can act as wetting agents and thickeners has gotten a lot of interest in recent years since their gelling ability enables for the formation of strong emulsifiers and gels by reducing interfacial and external stress while boosting liquid fluidity.

2. TYPES OF EMULGEL



3. RATIONALE OF EMULGEL

On the market, there are several semisolids and other preparations for restoring the skin's essential role or pharmacologically modifying an operation on the underlying tissue. Lotions, ointments, and creams, for example, have some problems, including being sticky, having a low spreading coefficient, and having stability concerns. Due to general limits within semisolid preparations, only clear gels are exposed in pharmaceutical and cosmetic preparations. As a result, to alleviate this constraint, an emulsion-based method is taken. As a result, the drug's hydrophobic moiety should be integrated and delivered via gels[7]. Hydrophobic drugs can be incorporated into emulgel's using drug/oil/water emulsions. Most medications cannot be placed directly into gel bases due to solubility, which causes issues during drug release. The technique facilitates the assimilation of an aquaphobic drug into the oil phase, followed by easy dissemination of oily blobs into the liquid form, leading to the development of oil/water emulsion. The gel base can be combined with the emulsion. When compared to just integrating the medication into the gel foundation, this may result in improved drug stability and release[8].



4. COMPONENTS OF EMULGEL

4.1 Oil Phase

Oily factors are needed for the emulgel's oily phase to form. Mineral oils, either alone or in combination with smooth or hard paraffin, are the most often used oils for topically applied emulsions. It functions as a carrier for the medication as well as its occlusive and sensory properties. The oil phase can include a wide range of lipids, both natural and manufactured. These lipids can range in consistency from mobile liquids to solids. Different oils are employed in formulations depending on their use, characteristics, and utility[9].

4.2 Vehicles

These two aquaphobic and hydrophilic drugs are employed in the emulgel formulation, as well as oily and watery carriers. In aqueous phase emulsions, carriers such as alcohol, water, and other aqueous components are employed.

4.3 Emulsifying Agent

The choice of Surface-active agents is based not only on their capacity to emulsify, but also on their route of administration and, as a result, their toxicity. The HLB number assigned to each surfactant represents the relative proportions of the lipophilic and hydrophilic sections of the molecule. A surfactant with a high number has mostly hydrophilic or polar qualities, whereas a surfactant with a low number has mostly lipophilic or non-polar properties. Emulsifying chemicals are required to promote real emulsification during manufacturing and to assure emulsion stability during the product's shelf life. The selection of an adequate emulsifying agent and its proper concentration is a question of trial and error. Tween 20 was used as an emulsifier in the aqueous phase of Emulgel, while span 20 was used in the oily phase. Polyethylene Glycol Stearate, Sorbitan Monooleate, polysorbate 80, Stearic Acid, and Sodium Stearate are examples of emulsifiers[10].

4.4 Gelling Agent

These are the ingredients that give any dose form its consistency and give it a gelled structure. The gel–sols–gel behavior increases the system's stability and bioavailability. Many parameters, including pH, temperature, polymer concentrations, polymer modification or combinations, and the addition of cations or anions, might alter the system's stability. Natural (Gelatin, Xanthan gum), semi-synthetic (Carboxy methyl cellulose, HPMC), and synthetic gelling agents are the three categories (Carbopol,) Polyacrylamide)[11].

4.5 Permeation Enhancer

Permeation enhancers are substances that help penetrant absorb through the skin by temporarily thinning the skin's impermeability. These polymers ought to be biochemically inert, non-irritating, innoxious, or consistent with active ingredients and medicament, as well as colorless, odorless, bland, and inexpensive, to pleasant solvent qualities. Oleic acid, clove oil, and menthol are some of the permeation enhancers employed in the emulgel formulation.

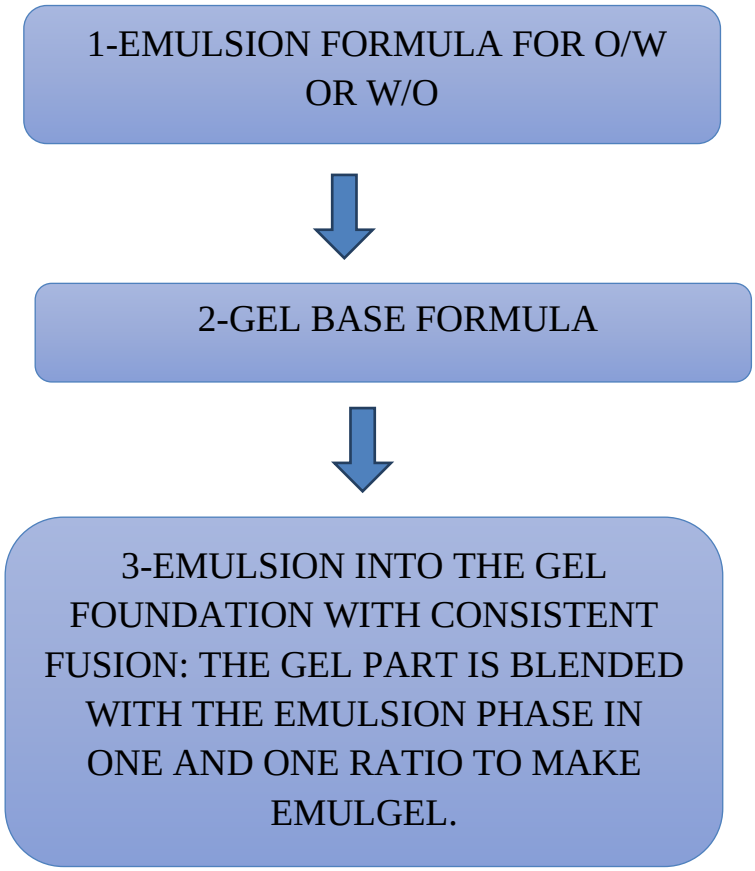
4.6 pH Adjustment

These substances are employed to keep the formulation's pH stable. Triethylamine, NAOH, and other similar compounds are examples.

4.7 Preservatives

These are the chemicals that stop or slow microbial, development, protecting the formulation from spoiling. Propylparaben, methylparaben, Benzalkonium chloride, Benzoic acid, Benzyl alcohol, and other preservatives are routinely employed.

5. STEPS IN THE PROCESS OF MAKING EMULGEL



The first steps in the production of an emulsion are the dissolving of oil-soluble chemicals in the oil vehicle (e.g., dissolve span 20 in liquid paraffin) and the dissolution of water-soluble compounds in the aqueous media (e.g., dissolve tween 80 in filtered water). Two phases were joined under vigorous mixing conditions to ensure the dispersion of two phases into droplets[12].In the laboratories, hydraulic stirrers are used to make emulsions, whereas, in industrial production, hydraulic stirrers, ultrasonics, high-pressure homogenization, or colloidal grinders are used to make emulsions[13].

The liquid medium's water-soluble ingredients or inert ingredients will be first dispersed in a nozzle by persistent swirling. To avoid aggregation, the hydrophilic polymers are carefully transferred to the agitated mixture and swirled until the polymer has dissolved and the pH stays inside the desired range[14]. The trapping of air in medicinal gels can be caused by excessive churning, hence the mixing rate should be kept to a minimum.

6 CHARACTERIZATION PARAMETERS

6.1 Physical Assessment

The created emulgel composition's appearance, coloration, homogenization, grittiness, texture, and phase partition were all perceivablyassessed[15].

6.2 pH Assessment

The pH of a developed emulgel is gaged using a digitized pH scale. To make a 1 percent aqueous solution of emulgel,1gram of emulgel is fused in 100 ml purified water and thoroughly agitated until it forms a homogeneous suspension. The system was left undisturbed for two hours. The pH is tested in triplicate after 2 hours by dipping the glass electrode in the suspension and calculating the average values[16].

6.3 Emulgel globule size and dispersion

An optical Microscope was used to determine the size and distribution of the globules. The globules are examined under a compound microscope with a magnification of 40 times. Before observation, the micrometer lenses validated with a stage micrometer as well as a stabilizing effect is established. The average globule sizes are then calculated[17].

6.4 Spreadability

A greater spreadability is among the desired features of an emulgel. It's a phrase for the area where emulgel spreads easily after being applied to the skin or damaged area. Multimer developed a spreadability measurement device consisting of a hollow cylinder fastened with one end by a rope. The emulgel's 'Slip' and 'Drag' qualities are used to determine spreadability. On this block is a ground glass slide. On this ground slide, around 2 grams of prepared emulgel is applied. The dosage form is then compressed between this slide and a second coverslip with the same proportions as the applied center point slide, as well as the hook. A 1-kilo load is placed on top of the two plates for around 5 minutes to evacuate air and create a homogeneous emulgel coating between the two slides[18].

6.5 Index of Swelling

1g of emulgel is placed on thin tinfoil and then allowed to stand in a 50 ml volumetric flask having 10 milliliters of 1.0 M NaOH to estimate the swelling index. After that, samples were taken from beakers at various time intervals and placed in a dry place for a while before being reweighed[19].

SW%= [(Wt-Wo)/Wo] *100 ……. Eq. (1)

Where (SW)%=Equilibrium percent swelling

Wt = Swollen Emulgel Weight after time t

Wo=Initial weight of Emulgel at zero time

6.6 Extrusion of Emulgel

The amount of force needed to eject the material from the cylinder is commonly measured using an empirical test. The procedure for calculating the amount of based intervention in the rheologic area that corresponds to loading stress larger than the optimum value and results in flow rate. The weight in grams necessary to produce at least 5 mm sash of emulgel in ten seconds was used to evaluate emulgel formulations for capacity to meet in this study. Relieved improves as the amount of material ejected grows. The extrudability of each formulation is tested three times, with the mean prices reported[20].

6.7 Drug Content

1g emulgel diluted in an appropriate solution until a transparent solution is obtained, then filtered. By using Ultraviolet spectrophotometry, can access wavelength. In the same solvent, a drug's standardized plotting is created. The amount and drug load can be assessed by examining the value of absorbency on the very same standard curve[21].

Drug content = (Concentration *Dilution factor*Volume taken) * (Conversion factor) ------Eq. (2)

6.8 *In vitro* Drug release

A Franz diffusion cell is used in the in vitro drug release research. An emulgel formulation is prepared and applied to the surface of a dialysis membrane that is fastened between the donor and receptor compartments of a Franze Diffusion cell. To solubilize the drug, a newly produced phosphate buffer solution with a pH of pH 7 is used as the disintegrating media and delivered within the cuvette. A circulating water jacket keeps the temperature of the Franze Diffusion cell at 37°C.For continuous stirring, the assembly is retained on a magnetic stirrer. A 5 ml sample was taken at appropriate stages and then refilled with an equivalent volume of new disintegration media to maintain the sink state. The stock solutions are examined with a Colorimetric Method set to a particular frequency, and the amount of drug release is calculated as time-dependent[22].

6.9 Microbiological Assay

The method of ditching plates is used to test a compound's Bactericidal or fungicidal properties. It's primarily used in semisolid preparations. Sabouraud's agar-dried plates that had been previously prepared were employed. In a trench cut in the plate, three grams of emulgel are inserted. Freshly produced growth loops are smeared across the agar at a straight angle from the hole to the plate's edge. After 48 hours of incubation at 25°C, the fungal growth was assessed and the % inhibition was calculated as follows[23].

% Inhibition =L2/L1*100 ----------Eq. (3)

Where L1 =total length of the streaked, L2=Length of Inhibition

7. FUTURE PROSPECTIVES

The aquaphobic behavior of medications, which eventually leads to poor aqueous solubility and pharmacokinetic concerns, is a common issue faced throughout the formation and execution of any unique dosage form. It has proved challenging to administer many drugs to the biological process because they are aquaphobic Different forms of medication delivery techniques that have been used topically include moisturizers, lotions, and different cosmetics preparation. Due to the presence of oily bases such as petroleum jelly, honey waxes, or vegetable oils, which are aquaphobic and do not enable the addition of an aqueous phase, they offer good demulcent characteristics but sluggish medication release. The gel increases faster medication release in contrast to certain other topical drug delivery system (TDDS) methods since it provides an aqueous environment for medicines. Hydrophobic drugs can be mixed into oily bases and given to the skin via emulgel. All of these advantages of emulgel over other topical medication delivery technologies make them more effective and profitable. In the future, these qualities will be used to transfer a greater range of topical drugs such as emulgel.

8. CONCLUSION

The goal of this literature study was to investigate how to make emulgel formulations. Several studies cited in this review have demonstrated that emulgel was developed and its usefulness as a uniquely effective drug delivery method to deliver medications. Furthermore, the review summaries the recent studies on emulgel's and emulgel's that are utilized to deliver plant extracts in medicinal applications, as well as herbal preparations. Several researchers have been using emulgel as an innovational drug delivery approach to deliver medicament to localized and extensive areas. Designed emulgel's have shown excellent results in terms of actualization, homogeneity, viscosity, amount of drug that passes into the epidermis, the release of drugs, and healing efficiency. All of these features make emulgel more effective and commercially viable than alternative topical drug delivery system. These physical and physicochemical qualities will be used to deliver a wider range of topical drugs in the future, including emulgel.

9. ACKNOWLEDGEMENT

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Table 1: List of Oils

Name of Oils	Properties
Olive oil	Antioxidant, Antimicrobial
Castor oil	Topical NSAIDs, Antioxidants
Myrrh oil	Antifungal, Antiviral
Balsam oil	Antifungal, Topical antibiotics
Wool Wax	Antimicrobials, Antifungal
Birch oil	Topical NSAIDs, Corticosteroids
Isopropyl myristate	Drugs for acne, Topical steroids

Table 2: List of Gelling agents

Gelling agent	Concentration
HPMC	2.5%
PLURONIC ® F127	1-3%
CARBOPOL 934	1%
COMBINATION OF HPMC AND CARBOPOL	1.2%
NaCMC	3-4%
PEMULEN	0.1-0.4%
CARBOPOL 940	1%

Table 3: Recent Studies on Emulgel Preparation

Active pharmaceutical drug	Excipients	Application and uses	References
Pomegranate extract-loaded Solid lipid nanoparticle	Stearic acid, Disodium hydrogen phosphate, Potassium dihydrogen phosphate, Tween 80, Carbopol 940, Ellagic acid.	The selected PE-SLNs emulgel formulation on mice with a solid tumor on their skin had statistically significant anticancer benefits.	[24]
Clove and Cinnamic Supercritical fluid extract	Tween 80, PEG-400, Almond Gum, Clotrimazole.	Herbal educe-loaded emulgels could be seen as a progression of polyherbal formulations, they could be another backup to present allopathic medications for treating denture stomatitis, which is having no side effect.	[25]
Oryza sativa extract	HPMC, Carbopol 940, Tween 80, Propylene glycol, Triethanolamine.	The active compounds in O. Sativa that serve as antioxidants and protect against UV radiation have a mechanism of action.	[26]
Albizia Lebbeck bark extract	Liquid paraffin, Propylene glycol, Carbopol 940, Span 20, Tween20, Methylparaben.	Antioxidants are extensively utilized in cosmetic goods because they benefit the skin and protect it from damaging environmental effects. Albizia lebbeck's antioxidant activity makes it a promising candidate for use in cosmeceuticals.	[27]
Nano-sized resveratrol nasal emulgel	Carbopol 934 and Poloxamer 407 were used as gelling agents, whereas Tween 20, Capryol 90, and Transcutol were used as surfactants and co-surfactant in various ratios.	The improved nasal nano emulgel demonstrated intranasal safety and increased bioavailability, making it a well-designed solution for brain targeting.	[28]

Dexibuprofen	Carbopol 940 was used as a gelling agent, as a penetration enhancer, and clove and Mentha oils were utilized.	Dexibuprofen's topical emulgel has an effective anti-inflammatory and analgesic effect.	[29]
Colchicine Niosomal Is Loaded into Jojoba Oil	Poly ethylene glycol-distearoyl phosphatidyl ethanolamine, Sorbiton monostearate, Tween 80, Span 60**.**	A combination of niosomal preparation and jojoba oil-based emulgel could indicate improved delivery of anti-inflammatory drugs like colchicine.	[30]
Nifedipine	The oil is light liquid paraffin, and the surfactants are Sorbitan monooleate and Polysorbate 20**.**	Nifedipine Emulgel is used for Treatment of Anal Fissure Using Polymeric Emulsifiers.	[31]
Itraconazole	Xanthan gum and guar gum-natural gelling agent**.**	This gel shows antifungal activity and works against various fungi like candida Albicans, candidiasis.	[32]
Tamanu oil	Span 20, Span 80, Tween 20, Tween 80, Isopropyl myristate, PEG400, Olive oil, Oleic acid**.**	Tamanu oil potentiated new sericin emulgel of Levocetirizine: repurposing for topical administration against DNCB-induced atopic dermatitis.	[33]

Table 4: Marketed Formulation[34,35]

Brand name	**Active ingredient**	**Manufacturer**
Miconaz-H-Emulgel	Miconazole nitrate, hydrocortisone	Medical union pharmaceutical
Voltaren	Diclofenac-diethyl-ammonium	Novartis pharma
Excex	Clindamycin, adapalene	Zee Laboratories
Topinate gel	Clobetsol propionate	Systopic pharma
Catafalm emulgel	Diclofenac potassium	Novartis
Avindo gel	Azithromycin	Cosme pharma lab

Table 5: Recent advancements in the formulation of herbal emulgel

Formulations (API)	Purpose and findings of the study	References
Avena sativa extract	Prepared a stable emulgel formulation with phytoconstituents generated from ethanolic extract of Avena Sativa and tested their effect on several facial parameters such as the anti-pigmentation effect.	[36]
Coccinia grandis leaf extract	Prepared and tested the emulgel using Coccinia grandis leaf extract, finding that formulations were found to be stable and effective, with strong antibacterial activity.	[37]
Cucurbita pepo seed extract	Prepared and tested an emulgel using an extract from the seeds of the medicinal plant Cucurbita pepo incorporating Carbopol 940 as a penetration enhancer were perfect.	[38]
Hibiscus rosa-Sinensis extract	Prepared and assessed an emulgel preparation with a methanolic extract of Hibiscus rosa-Sinensis and concluded that the formulation OEG 4 was the best and had the most anti-inflammatory activity of all the ones they tested.	[39]
Saussaria lappa extract	The phytochemical profile, formulation stability, and wound healing effects of an emulgel made using the methanolic extract of the medicinal plant Saussaria lappa were all investigated. The created emulgel has been reported to have improved wound healing activity, regulated medication release, and stability.	[40]
Kigelia Africana extract	Created and assessed emulgel and cream-based formulations using ethanolic aqueous extracts of the medicinal plant Kigelia Africana fruits, and found that both formulations are safe, efficacious, and stable, with emulgel releasing 3 percent more medication in vitro than cream formulation.	[41]
Coriandrum sativum	Produced and evaluated an emulgel-based formulation including seed oil from the Coriandrum sativum plant, reporting that the formulation was optimized, had superior outcomes in vitro and in vivo and had good anti-inflammatory action.	[42]
Zingiber Officinalis extract	Developed and tested the emulgel with a methanolic extract of the medicinal plant Zingiber Officinalis rhizomes, and found that the formulation F3, which contained 5% sodium CMC, produced better results and had a 98 percent increase in antibacterial activity.	[43]

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