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THE CREATION AND ASSESSMENT OF NANOEMULGEL: AN INTRIGUING APPROACH

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Abstract: *Other dermal forms have serious drawbacks in water-hating (hydrophobic] drug distribution. This is tackled when emulsion-based technique is being used and coupled with the unique qualities of gel, thereby emulgel has received considerable attention as a potential drug delivery, which is viewed as a novel form of delivery and a hybrid of gel & emulsion. The purpose is to shed light on the creation of emulgel and summarize crucial facts such as usage, preparation, and assessment. It has a greater release rate than other products, is readily removed, spreadable, thixotropic, less sticky, and has a nice calming look, indicating substantial pharmacological value and is largely devoid of adverse effects. It is presently being employed to extend the administration of NSAIDS, anti-inflammatory drugs, Antifungal and anti-acne*

Keywords: *nanoemulgel, topical preparation, evaluation, preparation.*

INTRODUCTION

An emulgel is a medication preparation that combine the characteristics of emulsions and gels, creating a semi-solid system that incorporates both water-loving (hydrophilic] and oil-loving (lipophilic] components. This blend offers several benefits such as increased steadiness, improved skin feel, and regulate expel of active ingredient. For example, salicylic acid, is non-steroidal recognized for its analgesic, anti-inflammatory, antipyretic & platelet aggregation-inhibiting attributes, is frequently use in skin therapies. they are particularly effective for delivering water repellent medication like salicylic acid, as they have asset such as thixotropic, easy spreadability, prolong shelf life making them superior from traditional creams or gels in various cosmetic and therapeutic applications.

It provides a local administration approach that avoids the first-pass metabolism linked to systemic treatment. These mixtures come in the form of gels, creams, lotions, and ointments, each with special advantages. While ointments are good at facilitating

drug absorption, creams combine an organic and aqueous base for ease of application; lotions, on the other hand, are more aqueous and can cover larger areas, albeit at the expense of lower drug concentrations; and gels, which trap liquids in a network of colloidal particles to facilitate easy spreadability, may not be as effective at delivering drugs as traditional gels. Its advantages over emulsion + gel include improved skin feel, controlled release, and durability. As a whole, the product is crucial in dermatology for the effective, focused treatment of dermatological conditions with research focused on enhancing these systems to improve delivery, ease to patients, minimizing side effects. On the other hand, conventional creams and ointments frequently have disadvantages such as poor spreadability, poor invasion within the corneal layer or reduced consumer acceptance as an outcome of adhesion or the need for intense massaging. however, may work well for certain API that have trouble with things that love oil. To improve the solubility and assimilation of antimicrobial agents via dermatitis and reach deeper skin layers for improved therapeutic effects, they address these difficulties with the use of customized fluids and emulsifiers. gel with their colloidal particles encapsulating high levels of aqueous or hydro alcoholic liquids, improve drug dissolution and migration compared to creams or ointments but can be challenging for water hating API. To overcome problem by incorporating emulsion and form EG thus improve bioavailability, pharmacological effects and solubility while reducing drug dosages

A step further is NEG, which uses certain gelling chemicals to embed nanoscale emulsion droplets into a gel matrix. By preventing the degradation of active components and boosting stability through increased viscosity and decreased interfacial tension, this dual-phase system improves medication delivery. Because the emulsion droplets are tiny, the addition of penetration enhancers also increases drug permeability and spreadability.

SKIN PHYSIOLOGY

represents the largest unit in one's body, making up 15% of the total body weight of an adult., having crucial roles for safeguarding against physical, chemical, and biological threats, managing hydration, and assisting thermal control. As a continuous barrier, it connects with mucous membranes lining body's internal surfaces. It’s primarily made up of three layers.

epidermis: It lacks blood channel and consists of four distinct sheets of keratinocytes, which are cells at different stages of maturation. [1]

Cellular components distributed in Epidermis are:

1. **Stratum Basale**

   Often referred to as the stratum germinativum, it is made up of columnar keratin cells that adhere to the basement barrier region along a long axis that is perpendicular to the dermis. Desmosome junctions connect a single row of cells, connecting them to the squamous cells above. The dark stain, oblong or lengthened nuclei of basal cells are indicative of their presence of melanin pigment, which is transmitted from adjacent melanocytes. [2]

2. **Stratum Spinosum**

   Termed as prickle cell layer, encompasses 8-10 irregularly shaped, polyhedral cells with

cytoplasmic projections often referred to as "spines." Furthermore, compromise dendritic cells, involves in immune function. Desmosomes are plentiful in the spaces between spinous cells, providing strong mechanical connections that increase resistance to physical stress. [3]

3. **Stratum Lucidum**

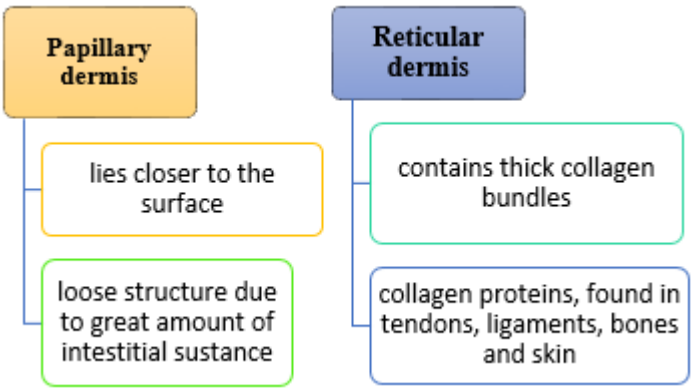
They are tailored part of epidermis, typically found in areas of thick parts like sole and palm. This translucent layer is composed of flat, densely packed dead cells with indistinct boundaries, which gives it a clear appearance when viewed under a microscope. In addition, be composed of protein called eleidin, contributes to the layer's translucency. Functionally, provides extra protection by serving as an additional protection against antigens, in particular water loss, mechanical abrasion, reduces friction between epidermal layers, maintain structural integrity and improve its resistance to physical stress. [4]

4. **Stratum Corneum**

Is outermost element. Main role is to provide a strong defence shield for the underlying skin layers. blocks foreign element from entering. [5]

Dermis:

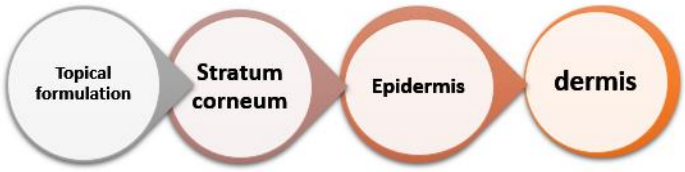
Divided into two main regions [6]



Hypodermis [subcutaneous layer]

Is deepest of all, positioned beneath the Dermis and above the muscles. It acts as insulator that regulate thermal state of a particular by trapping heat and reducing heat loss. It also serves as padding film disperses mechanical shock, protecting internal organs from injury. [7]

Drug penetration pathway for topical preparation:



2.3 EMULGEL:

it involves applying medications directly to various body surfaces, including the eyes, rectum, vagina, and skin, to treat healthy and diseased skin. explicitly made for dermatological use, offer notable benefits consisting of thixotropy, non-greasiness, ease of utilization and removal, moisturizer, non-staining nature, long shelf life, biocompatibility, transparency, and an aesthetically pleasing look.

This characteristic makes them highly effective for localized treatment, particularly when other delivery methods are inadequate [8]

Topical products are classified into two types. External products are applied directly to the upper surface to treat localized areas, while internals to mucous membranes in the mouth, rectum, or vagina for therapeutic effects. It preferred method to treat condition like acne, eczema, and psoriasis due to its direct application to affected part and ongoing advancements in technologies aimed at improving outcomes and patient adherence. [9]

Gels are a modern form of administration that improve dissolution and migration over ointments or creams but have challenges in effectively delivering drugs. They are made by trapping large amounts of fluid or hydro-alcoholic substances within a network of colloidal particles, which can be either organic or inorganic. [10]

Particularly emulgels, has grown due to their homogeneous consistency and gel-like properties. Also known to be O/W emulsion or cream gels, they began to gain prominence. Nanoemulgels, an advanced form, use nano-sized emulsion droplets within a gelatinous matrix, increases drug penetrating power by help of concentration gradient [11]

Nanoemulgel = nanoemulsion + gel

Emulsion

Emulsions are formed by mixing no. of liquids that normally do not mix, such as oil and water. That got mix with the help of emulsifier and maintaining the stability of the mixture also ensuring its uniformity. they are valued for their ease of removal and effective skin penetration. [12]

Nanoemulsion

They are highly stable, optically clear colloidal systems with droplet sizes typically under 100 nm. They consist surfactant, often with a co-surfactant, resulting in a thermodynamically steady formulation. O/W are particularly effective for delivering nonpolar structures or bio-active compound into deeper layers, making them ideal for targeting the lyophilic environment of the pilosebaceous unit, beneficial for acne and psoriasis. [13]

Gel

This term describes that improving viscosity while maintaining its characteristics. It serves as thickening agents, improving consistency and uniformity. Typically made from polymers that swell in the presence of fluids, they can be mixed with emulsions to create an emulgel. These jelly trap liquid within their structure, resulting in smooth and wet texture. [14]

RATIONALE BEHIND USE OF EMULGEL

Some former composition like lotion, ointment, and cream may contain challenges, including stickiness that can irritate patients, inefficient spreading, and the need for rubbing during application, they are not stable too and to overcome these problems, there has been a shift towards using transparent gels. They are colloidal systems where about 99% of the content is watery, stabilized by surface tension within a macromolecular fibre mesh made by a small quantity of gelling agent. Given that about 40% of

therapeutically active compounds is nonpolar, forming them in gels is hard. Emulsion-based gels, or emulgel, provide a solution by increasing solubility and penetration water hating substances. Also improves pharmacological effects and decreasing the necessary dose by facilitating better access of medicines globules into soft tissues. [15]

Advantages of emulgel

1. Lipid loving drugs implemented easily in the gel base.
2. Target drug delivery on the body
3. Easy for production and a low-cost mechanism.
4. Avoid sonication.
5. The first metabolism is avoided.
6. Avoid gastrointestinal incompatibility.
7. Improved stability and load capacity.
8. Improved patient compliance.
9. Improved patient acceptability and suitability for self-medication.
10. Ability to easily terminate medication [16]

Disadvantages of emulgel

1. The drug and/or excipients can lead to skin irritation in people with contact dermatitis.
2. Some medications have low permeability through the skin.
3. Possibility of allergenic reactions.
4. Larger-particle-size drugs are not easily incorporated into the skin [17]

MATERIALS AND METHODS

Basic component of emulgel

Every component needs to be deemed generally regarded as safe [GRAS], soothing, non-sensitizing, and approved by pharmaceutical companies. The role of each ingredient in, is critical to achieving the desired properties and overall performance of the product.

1. ***Active ingredient:***

   Show clinical effects and is biologically active. APIs are essential in medications, delivering the intended benefits. Salicylic acid is a notable substance used to treat psoriasis and other skin conditions.

2. ***Emulsifier***

   Essential for creating and maintaining the stability, commonly include Polyethylene glycol 40 stearate,

3. ***Water:***

   Makes other phase of mixture and also used to form solid mucilage components into semisolid.

4. ***Gelling agent:***

   They transform the emulsion into a thixotropic system, improving the texture and quality of the final product. Ex carbopol, HPMC etc.

5. ***Penetration enhancer:***

   Have low irritancy and toxicity while improving drug penetrability. These agents work through various mechanisms, such as temporarily disrupting the upper barrier, fluidizing the lipid channels between keratinocytes, and modifying the partitioning within the lipid structures. By using suitable excipient, the efficiency of distribution of

particles is improved, enhancing therapeutic outcomes.

Preparation of emulgel:

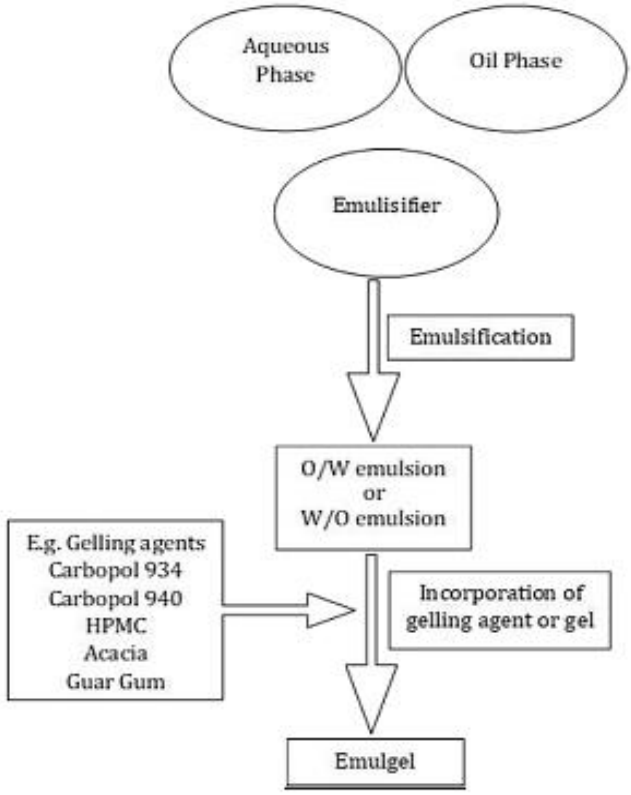
Step 1: formulation of o/w emulsion:

When it comes to the first step, water-soluble materials are dissolved in an aqueous solution [like Tween 80 in filtered water] and oil-soluble materials are dissolved in an oil vehicle [like Span 20 in liquid paraffin]. To aid in the dispersion of one phase into droplets within the other, a mechanical stirrer is used to blend these two phases. [18]

Step 2: formulation of gel base

Form by gelling agent [gelatin, HPMC] it is dissolved in water for 24 hr. get swelled and mixed into magnetic stirrer to loose lumps and form smooth elegant texture in gel form [19]

Step 3: Steady blending to form EG



RESULT AND DISCUSSION

Evaluation of emulgel

***Skin irritation study*:** it is also known as patch test, mainly done over small exposed area of rats where preparation applied and changes are observing like morphology of skin and color in particular time period [20]

Zeta potential: after dilution of preparation suitably with deionized water, zetasizer instrument is used for measurement of particle potential after result cuvettes are washed [21]

Ph measurement: The supersaturation approach was used to pH solubility experiments. Using a conical flask, 5 mL of the medium was introduced, followed

by little additions of pure drug, until saturation was achieved. Next, the solutions were subjected to a 24-hour mechanical rotary shaker shake. The drug solutions in the different medium were then centrifuged, and the filter was placed over the supernatant. The solubility of the filtered solutions was then determined by diluting them accordingly and recording the drug's maximum absorbance in each medium. [22]

Solubility: The drug's saturated solubility in water was examined in tests conducted on the drug, its produced formulations, and its lyophilized form. In a bath at 37 °C, an excess of the dry powder formulations was suspended in the current volume of water and agitated for 48 hours at 100 revolutions per minute [until equilibrium solubility was reached]. The samples were then suitably diluted following the allotted time. To eliminate any excess solid, the sample was ultracentrifuged for 15 minutes at 15,000 rpm. The drug concentration was then measured using UV spectrophotometry set at 240 nm. The equation derived from the drug's constructed in distilled water was used for determining the concentration of the dissolved medication. A comparison was made between the formulations that had the highest solubility and those that had the same drug to stabiliser ratio in a physical combination. For every formulation, three runs of the test were conducted.

Spreadability: it is important study for dermatological formulation which cause ease in application over epidermis or other affected reason this attribute has significant importance since it has the potential to impact medicinal efficacy

Each sample was put between to glass slides in triplicate to quantify spreadability the lower plate is loaded with 0.5gm of sample, plate was layered over it and force is created in one-minute time interval and spreadability is measured by the formulae: Weight× Distance/ time [23]

Drug- excipient compatibility: this study of drug and various excipient is done to know physical and chemical incompatibility under stress condition where they are taken in 1:1 for 15 days and physical appearance is observed

Drug release study: there are many ways to measure drug release of formulation like In-vitro, Ex-vivo, In-vivo

1 gm of drug is placed over cellophane membrane in Franz diffusion cell and clamped between receptor and donor chamber where receptor was filled freshly prepared buffer at pH 7.4 to solubilize the drug stirred at 50 rpm maintain temperature of human body sample are analysed by using a uv- visible spectrophotometer [24]

CONCLUSION

Traditional transdermal administration techniques have considerable delivery challenges when dealing with lipophilic compounds due to their insufficient epidermal penetration and highly limited therapeutic effects. According to scholarly research, the formation may enhance medication permeab. by upsetting the bilayer on the skin. With respect to other systems, nanoemulsion exhibits a higher capacity for drug solubility and a higher degree of

thermodynamic stability, which makes it a promising carrier delivery method for polar treatments. Combining the hydrogel and nanoemulsion systems results in a longer shelf life and requires less energy during manufacturing. Both methods have some limitations: lipophilic compounds cannot be included in hydrogels, while NE have poor retention and low spreading properties. With NEG, the drawbacks of both approaches can be circumvented. The hydrogel basis is mixed with the oil phase that makes up the NE, which includes the lipophilic medication. This allows one to add a lipophilic medication to a hydrogel while simultaneously increasing the viscosity. It is used in cutaneous medication to reserve; the medication initially enters the outer phase before moving into the skin's surface from the inner step. Following application to epidermis, beads go from the gel matrix of the NEG. These droplets went on to deeply penetrate the corneum, directly delivering the API.

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