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Review Article

Emulgel and Nano Emulgel as Topical Drug Delivery System

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ABSTRACT

Emulgel is an innovative drug delivery system that combines the advantages of both emulsions and gels, offering a promising approach for enhanced topical drug delivery. This unique formulation integrates oil-in-water or water-in-oil emulsions into a gel base, enabling superior penetration of active pharmaceutical ingredients through the skin. The emulgel system enhances the solubility and bioavailability of lipophilic drugs, making it an ideal candidate for topical applications in dermatology, pain management, and anti-inflammatory treatments. Its dual-phase structure allows for controlled drug release, improved stability, and enhanced patient compliance due to its non-greasy, easy-to-apply nature. This paper reviews the key advantages of emulgels, formulation techniques, and their potential in overcoming the limitations of traditional topical drug delivery systems. Emulgel is emerging as a versatile and efficient platform for delivering therapeutic agents with enhanced efficacy and safety profiles. Nano-emulgel a cuttingedge drug delivery system aimed at enhanced the therapeutic effectiveness of lipophilic medication. This innovative formulation merge nano emulsion with enabling both immediate and sustained drug release which is topically face challenges such as poor solubility inconsistent absorption and low oral bioavailability. The growing interested in nano emulgel is due to its capacity for targeted delivery convenience of application and avoidance of gastrointestinal degradation along with useful and productive outline. Topical drug delivery systems play a crucial role in treating localized and systemic infections. Among various dosage forms—creams, ointments, gels, pastes, and lotions—emulgels have emerged as a promising alternative, particularly for delivering hydrophobic drugs. This review explores the properties, advantages, and formulation considerations of emulgel.

INTRODUCTION

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Emulgels are innovative formulations that combine the characteristics of gels and emulsions. They provide a dual release control mechanism, allowing for effective drug delivery through both gel and emulsion phases. This unique combination enhances the solubility of hydrophobic drugs, making them more bioavailable when applied topically. Topical drug delivery systems have gained significant attention in recent years due to their ability to deliver therapeutic agents directly to the site of action, minimizing systemic side effects and improving patient compliance. However, traditional topical formulations such as creams, ointments, and lotions often suffer from limitations like poor drug penetration, low stability, and greasy feel, which can affect both efficacy and user experience. To address these challenges, a novel approach called emulgel has emerged, combining the properties of emulsions and gels into a single formulation. Emulgels are unique in that they incorporate emulsified drug systems within a gel matrix, offering the benefits of both forms. Emulsions (either oil-in-water or water-in-oil) facilitate the incorporation of both hydrophilic and lipophilic drugs, while gels provide a non-greasy, aesthetically pleasing texture that enhances the ease of application and absorption. This hybrid system allows for better drug solubility, enhanced skin penetration, and sustained release, making it an ideal candidate for delivering a wide range of therapeutic agents topically.

The lipophilic properties of these drugs lead to issue such as inadequate solubility, unpredictable absorption and variability pharmaceuticals along individuals. Recent advancement in pharmaceutical synthesis and rapid screening techniques have shifted pharmaceutical discovery and development towards hydrophobic compound currently, 99% of medications in the development pipeline and over 40% of existing drugs are hydrophobic in nature. A variety of strategies have

been implemented to enhance the solubility of active substances. These strategies involve both physical and chemical alterations of active pharmaceutical ingredients along with formulation method like size reduction, complexation, amorphization and nano-carrier delivery system. Furthermore, clinical issues and low drug concentration at the site of action hinder effective oral delivery, for example, the oral use of disease Modification anti-rheumatic drugs, [DMARD] for treating arthritis is linked to significant side effects including carcinogenicity and haematological toxicity. Despite using various methods to enhance solubility, administering drug through the oral way is not always viable due to low bioavailability related to inadequate absorption, first pass metabolism, and chemical or enzymatic degradation. This clinical challenge can be addressed by delivering the drug through tropical route for drug delivery. This introduction highlights the rising importance of emulgel formulations in overcoming the limitations of conventional topical drug delivery. In the following sections, the formulation techniques, benefits, and potential applications of emulgels in pharmaceutical and cosmeceutical fields will be explored in detail.

Properties of Emulgels

Thixotropic: Emulgels exhibit a reversible gel-to-liquid transition upon shear stress, allowing for easy application and spreadability.

Greaseless: Unlike traditional ointments, emulgels do not leave a greasy residue, making them more acceptable for users.

Easily Washable: They can be easily removed with water, enhancing user convenience.

Emollient: Emulgels provide moisturizing effects, which are beneficial for skin health.

Non-Staining: Their formulation typically avoids leaving stains on clothing or surfaces.

Long Shelf Life: Emulgels tend to have stable formulations, contributing to extended shelf life.



Transparent Appearance: The clarity of emulgels enhances their aesthetic appeal, making them suitable for apply on the skin.

Advantages of Emulgels

- **Enhanced Drug Solubility:** Emulgels facilitate the delivery of hydrophobic drugs, overcoming a major limitation of traditional gels.
- **Controlled Release:** The dual mechanism allows for sustained and controlled release of active ingredients, improving therapeutic efficacy.
- **Versatility:** Emulgels can be formulated for various therapeutic uses, including pain relief from injuries, arthritis, headaches, muscle aches, and backaches.
- **Patient Compliance:**
 - Their pleasant texture and ease of application can lead to higher patient adherence to treatment regimens.
 - Enhances drug penetration for improved efficacy.
 - Incorporates both hydrophilic and lipophilic drugs.
 - Non-greasy, smooth texture for better patient compliance.
 - Allows for controlled or sustained drug release.
 - Provides increased stability and longer shelf life.
 - Aesthetically appealing and easy to apply.
 - Spreads evenly, enhancing drug absorption.
 - Offers moisturizing benefits for skin applications.
 - Targets local areas, minimizing systemic side effects.
 - Less irritation compared to oil-based formulations.
 - Rapid skin absorption for faster onset of action.

- Flexible in formulating various drugs.
- Cost-effective and simple to produce.

Disadvantages

- Limited drug load capacity in some cases.
- Potential skin irritation from certain ingredients.
- Complex formulation process for consistency and release.
- Stability issues for certain sensitive drugs.
- Short duration of action for some drugs, requiring frequent application.

Formulation Considerations

When developing emulgels several factors must be taken into account:

1. **Choice of Gelling Agent:** Selecting appropriate gelling agents (like carbomers or xanthan gum) is crucial for achieving desired viscosity and stability.
2. **Emulsifying Agents:** The selection of emulsifiers (such as polysorbates) impacts the stability of the emulsion phase and overall performance of the emulgel.
3. **Active Ingredients:** The solubility and compatibility of the active pharmaceutical ingredient (API) must be evaluated to ensure effective delivery.
4. **pH and Ionic Strength:** The formulation's pH and ionic conditions can influence the stability and drug release profiles of emulgels.
5. **Preservatives:** Given that emulgels may contain water, appropriate preservatives are often needed to prevent microbial growth.

Rationale of emulgel as a topical drug delivery system

Emulgel offers a unique advantage as a topical drug delivery system by combining the strengths of emulsions and gels. Traditional topical formulations often suffer from poor drug penetration, stability issues, and greasy textures that can hinder patient compliance. Emulgel



addresses these challenges by integrating a gel-based system that provides a non-greasy, easily absorbable formulation, while the emulsion allows for the incorporation of both hydrophilic and lipophilic drugs, thus enhancing the solubility and bioavailability of a wide range of therapeutic agents. The gel matrix ensures better stability, controls the release of active ingredients, and enhances skin penetration. These properties make emulgel a superior alternative for delivering drugs locally, particularly for conditions requiring enhanced skin permeability, such as in the treatment of dermatological diseases, pain management, and inflammation. Its flexibility, ease of application, and ability to deliver drugs efficiently to the target site form the core rationale behind its development as a promising topical drug delivery system. Factors affecting topical absorption of drug-

Physiological Factors

- Improves the delivery of active ingredients through the skin.
- Incorporates both hydrophilic and lipophilic drugs.
- Prevents phase separation and prolongs shelf life.
- Allows sustained and consistent drug release for prolonged action.

Factors to be considered when choosing a topical preparation

- **Drug Properties** Consider the solubility, stability, and molecular weight of the active ingredient, as these factors influence its absorption and effectiveness through the skin.
- **Formulation Base:** Evaluate the type of base (e.g., ointment, cream, gel, emulgel) to determine it
- **Skin Condition and Area:** Assess the condition of the skin (e.g., intact, inflamed, or broken) and the specific area of application, as different

formulations may be better suited for various skin types and conditions.

- **Patient Preference and Compliance:** Take into account the patient's preferences regarding texture, scent, and ease of application, as these factors can significantly affect adherence to the treatment regimen

- Match the type of preparation with the site. (e.g., gel or lotion for hairy areas)
- Irritation or sensitization potential. Generally, ointments and w/o creams are less irritating, while gels are irritating. Ointments do not contain preservatives or emulsifiers if allergy to these agents is a concern.

Drug delivery across the skin

Transcellular Route:

Drugs penetrate directly through the cells of the stratum corneum, moving through the lipid bilayers and keratinocytes. This route is commonly utilized for smaller, lipophilic molecules.

Intercellular Route:

Drugs diffuse through the spaces between skin cells. This route is significant for hydrophilic drugs and is facilitated by the presence of intercellular lipids that can influence permeability.

Transappendageal Route:

Drugs can also penetrate through hair follicles and sweat glands. Although this route accounts for a smaller percentage of overall absorption, it can be significant for certain infections and pain by medication. New technologies now allow other drugs to be absorbed through the skin. These can be used to treat not just the affected areas of the skin but the whole body by systemic route

Emulgel preparation aqueous material

Emulgels are topical formulations that combine the benefits of emulsions (oil-in-water or water-in-oil) and gels, offering a unique texture and enhanced drug delivery properties. The preparation of emulgels typically involves



incorporating an aqueous phase into an oil phase, along with gelling agents and other excipients. Here's a general outline of the preparation process, specifically focusing on the aqueous materials involved-

Emulsifiers

Emulsifiers are substances that stabilize emulsions, which are mixtures of two immiscible liquids, such as oil and water. They play a crucial role in various industries, including food, pharmaceuticals, and cosmetics, by ensuring uniform dispersion of ingredients and improving the stability and texture of formulations.

Gelling agent.

Table 2: Use of gelling agents

Gelling agent	Quantity	Dosage form
Carbopol-934	0.5%-2%	Emulgel
Carbopol-940	0.5%-2%	Emulgel
HPMC-2910	2.5%	Emulgel
HPMC	3.5%	Gel
Sodium CMC	1%	Gel

Table 3: Use of penetration enhancers

Penetration enhancer	Quantity	Dosage form
Oleic acid	1%	Gel
Lecithine	5%	Gel
Urea	10%	Gel
Isopropyl myristate	5%	Gel
Linoleic acid	5%	Gel
Clove oil	8%	Emulgel
Menthol	5%	Emulgel
Cinnamon	8%	Emulgel

Gelling agents are substances used to create gels, which are semi-solid materials that exhibit both liquid and solid properties. They play a crucial role in various industries, including food, pharmaceuticals, and cosmetics, by providing structure, stability, and desirable textures to formulations.

Permeation enhancers

Permeation enhancers are substances that facilitate the absorption of drugs through biological

membranes, particularly the skin, by modifying the barrier properties of the stratum corneum. They are crucial in enhancing the bioavailability of topical and transdermal formulations, making them particularly valuable in pharmaceutical and cosmetic industries.

Properties of penetration enhancers

- **Mechanism of Action:**

Effective penetration enhancers work by altering the structure of the stratum corneum, disrupting lipid bilayers, or creating channels that facilitate drug transport through the skin.

- **Biocompatibility:**

They should be safe for use on human skin, causing minimal irritation or allergic reactions, and should not produce adverse systemic effect.

- **Solubility:**

A good penetration enhancer should be soluble in both the formulation and the skin barrier, allowing for efficient interaction with the drug and skin lipids.

- **Stability:**

The enhancer should remain stable under varying environmental conditions (e.g., temperature, pH) during the shelf life of the product.

Mechanism of penetration enhancers

- **Disruption of the Stratum Corneum Lipid Structure:**

Fluidization: Many penetration enhancers alter the lipid bilayer of the stratum corneum by disrupting the packing of lipid molecules. This fluidization allows for increased drug permeation by reducing the barrier function of the skin.

Lipid Solubilization: Some enhancers can solubilize the lipids in the stratum corneum, creating a more permeable pathway for drug molecules.

- **Creation of Micro-channels:**

Microneedles: Certain mechanical enhancers, like microneedles, create microchannels in the skin that facilitate the transport of larger drug



molecules directly into the dermis, bypassing the stratum corneum entirely.

- **Increasing Skin Hydration:**

Hydration Effects: Enhancers that increase the moisture content of the skin can swell the stratum corneum, making it more permeable. This can be achieved through the use of humectants or occlusive agents that trap moisture.

Preparation of emulgel

The preparation of emulgel involves a systematic process that combines an aqueous phase with an oil phase, incorporating gelling agents to create a stable formulation suitable for topical application. First, the aqueous phase is prepared by heating purified water and gradually dispersing a hydrophilic gelling agent, such as carbomer or hydroxypropyl methylcellulose (HPMC), while stirring continuously to avoid clumping. In a separate container, the oil phase is created by mixing oils, such as mineral or olive oil, with lipophilic emulsifiers like glyceryl monostearate, followed by gentle heating to ensure uniform blending. The oil phase is then slowly added to the aqueous phase while stirring vigorously to form a stable emulsion, which is subsequently cooled. As the mixture cools, the gelling agent hydrates, thickening the emulsion into an emulgel. Any heat-sensitive active ingredients or fragrances are incorporated at this stage to ensure even distribution. Finally, the emulgel is homogenized to achieve a smooth consistency, and its pH is adjusted to ensure skin compatibility. The prepared emulgel is then filled into suitable containers under aseptic conditions, ready for use in therapeutic or cosmetic applications.

Evaluation of emulgel Fourier transforms infrared spectroscopy (FTIR)

The primary objective of this investigation was to identify a stable storage condition for the drug in solid state and identification of compatible excipients for formulation.

Physical examination

The Prepared emulgel formulations were inspected visually for their colour, homogeneity, consistency and phase separation. **Determination of pH**

pH of the formulation was determined by using digital pH meter. pH meter electrode was washed by distilled water and then dipped into the formulation to measure pH and this process was repeated 3 times.

Measurement of viscosity

The measurement of viscosity is a critical aspect in evaluating the flow behaviour and stability of emulgels and other formulations. It can be performed using various methods, primarily employing viscometers and rheometers. A capillary viscometer measures viscosity by timing how long a liquid takes to flow through a glass tube, while a rotational viscometer determines the torque needed to rotate a spindle in the sample, providing direct viscosity readings. Oscillatory rheometers can also be used to assess the viscoelastic properties of the emulgel. Viscosity can be expressed as dynamic viscosity, which indicates the internal resistance to flow, or kinematic viscosity, which factors in the fluid's density. Measurement conditions, such as temperature and shear rate, are crucial since viscosity can change under different circumstances. Before testing, samples should be prepared to ensure homogeneity, and instruments must be calibrated correctly. During measurement, multiple readings are often taken to ensure accuracy, with the results analysed to confirm that the emulgel meets the desired specifications for its application. Accurate viscosity measurement is essential for quality control, ensuring that formulations exhibit the intended flow properties and stability.

Spreadability

Spreadability is an important parameter for emulgels, particularly in topical applications, as it influences the ease of application, uniform



distribution, and overall effectiveness of the formulation on the skin. It refers to the ability of the emulgel to spread over a given surface area with minimal effort and is often assessed through various methods.

Swelling index

The swelling index is a crucial parameter in evaluating the performance of emulgels, particularly in terms of their ability to retain moisture and release active ingredients over time. It refers to the degree to which a gel or emulgel expands upon absorbing a solvent, typically water. This property is significant for topical formulations, as it affects drug release kinetics, stability, and overall effectiveness.

In vitro drug release study

In vitro drug release studies are vital for evaluating the performance of emulgels as topical drug delivery systems, as they simulate the release of active pharmaceutical ingredients (APIs) under controlled conditions. The primary objective of these studies is to assess how effectively and quickly a drug is released from the emulgel, providing insights into its potential therapeutic effectiveness. Typically, a Franz diffusion cell is used, where the emulgel is applied to a membrane in the donor compartment, and the receiver compartment contains a medium that mimics skin conditions, such as phosphate-buffered saline (PBS). The study is conducted at a constant temperature, usually 37°C, to simulate body temperature. Samples are taken at predetermined intervals from the receiver compartment to measure the concentration of the released drug, using techniques like UV-Vis spectroscopy or HPLC for analysis. The release data is then plotted against time to evaluate the release profile, with various kinetic models applied to understand the release mechanism. Factors such as the viscosity of the emulgel, composition, pH, and temperature can significantly influence drug release, making it essential to control these conditions throughout the

study. Overall, in vitro drug release studies are crucial for predicting the efficacy and behaviour of emulgels, guiding formulation development and optimization for improved therapeutic outcomes.

Microbiological assay

Microbiological assays are essential analytical techniques used to evaluate the antimicrobial activity of drugs, particularly in formulations like emulgels. These assays help determine the effectiveness of active pharmaceutical ingredients (APIs) against specific microorganisms, ensuring that topical formulations are not only effective but also safe for use. The primary goal is to assess the efficacy of emulgels and their active components in inhibiting the growth of bacteria, fungi, and other pathogens. Common types of assays include the Minimum Inhibitory Concentration (MIC), which determines the lowest concentration of an antimicrobial agent that prevents visible growth of a microorganism, and the agar diffusion method, where discs impregnated with the emulgel are placed on an agar plate inoculated with microorganisms to measure the zone of inhibition. The procedure typically involves preparing test tubes with varying concentrations of the emulgel mixed with nutrient broth and adding a standardized inoculum of the microorganism, followed by incubation. Results are interpreted based on the size of inhibition zones or the concentrations at which growth is inhibited, providing insights into the formulation's antimicrobial potency. Conducting microbiological assays is crucial for validating the safety and efficacy of topical formulations, ensuring that they effectively combat microbial contamination and do not pose a risk to users. Overall, these assays play a critical role in the development and quality control of emulgels and other pharmaceutical formulations, contributing to better therapeutic outcomes and consumer confidence in topical treatments.

Skin irritation test



Skin irritation tests are essential evaluations conducted to assess the potential irritancy of topical formulations, including emulgels, on the skin. These tests are critical in ensuring the safety and tolerability of dermatological products before they are approved for human use.

Stability studies

Stability studies are essential assessments conducted to evaluate the shelf-life and overall stability of pharmaceutical formulations, including emulgels. These studies determine how well a formulation maintains its quality, efficacy, and safety over time under various environmental conditions. In topical delivery, the skin being a primary protective barrier, perceive active pharmaceutical ingredients are external substance and within the absorption into the body various Method's have been investigated to enhance drug permeation converse. the use of acne carriers has to be an effective strategy for passing the stratum concern biggest without increasing skin damage out achieving efficient drug penetration on such approach in vote disrupting the structural integrity of the skip layer which can be achieved then the techniques such as chemical penetration enhance, ultrasound iontophoresis electroporation and Microneedles. These innovative carrier for topical administration include, but are not limited to emulsion, Micelles dendrimers life some Solid lipid nanoparticles carrier these carrier facilitate drug delivery through the skill by utilize, Inter cellular and transport Mechanism, interacting with skin component to aid transport of to create depots for sustained among these nano emulsions are considered a promising drug delivery system due to their high drug loading capabilities solubilizing properties each of production , stability and controlled release profile.

Additionally the stability of liposome has been a persistent concern, as they tend to disintegrated during the penetration process likewise micelles demonstrate poor stability and encapsulation

efficiency similarly the low drug loading capacity and uncontrolled release limit the application of solid and lipid nanoparticle in dermal drug delivery furthermore the toxicity and inadequate controlled released characteristics of determined restrict their topical uses. Nano-emulgel is a colloidal formulation that combines an emulsion and a gel offering a dual strategy for drug system. the gel component enhance viscosity and spreadability helping to maintain therapeutic concentration over time and improving skin adherence the emulsion element safeguards the compound from enzymatic degradation and hydrolysis while facilitating skin absorption Nano-delivery system. Additionally, it lowers surface and interfacial tension, thereby boosting thermodynamic stability overall nano-emulgel present a high capacity for drug loading enhanced and diffusion and reduced skin complexation compared to alternative nano-delivery system.

The article aims to insights into the selection of formulation material for nano-emulgel. its application and preparation consideration uses pharmacokinetics and pharmacodynamics as well as its shielded profile. the objective is to prospects and rationale for nano drug delivery system.

2. Drug delivery through a topical route.

The advantage of the topical administration route consist of avoiding the hepatic first pass effect ,diminished side effect due to localize action enhance percutaneous absorption and potentially increase bioavailability through prolonged deposition .The feature of any ideal formulation includes patients adherence self administrations non invasive methods furthermore reduced drug loss from metabolism or degradation and the ability to target the drug at specific locations and also notable benefit minimize drug breakdown ,combine with continuous delivery over on prolonged duration ,promotes the drug movements across the stratum corneum barrier ,leading to enhanced bioavailability .An increase in drug



bioavailability through the topical route has been shown in numerous studies for example flurbiprofen nano emulsion demonstrated a 4.4 fold rise in bioavailability with topical administration compared to oral delivery .GANNU ET AL .reported a 3.5 fold increase indicating that this improvement could result from avoiding the first pass effect during topical application .furthermore an enhancement and pharmacological impact of active agent has been evidenced with topical formulation .Standard topical formulation like solution ointments ,lotions ,creams patches and gels encounter considerable delivering agent through the skin. Its composition significantly hinders the effective penetration of active compounds .complication both topical and transdermal drug delivery .this evident in available topical product which shows lows permeations and results in limited therapeutical effectiveness.as a results research efforts have turned towards innovative carriers system designed to enhanced the permeability of hydrophobic drug through skin .the research in the domain primarily focuses on developing topical formulation with improved permeability through various method .and also the new production methods and strategies have surfaced a major drawback is the dependence on chemicals and non eco - friendly solvents to increase permeation .additionally despite the skin 's constraints ,contains attributes are necessary for an active ingredients to be appropriate for topical administration .

1. Composition

- **Conventional Emulgel:**
 - Composed of an emulsion (oil-in-water or water-in-oil) combined with a gelling agent (like carbomers).
 - Contains larger droplet sizes (typically in the micrometer range) for the dispersed phase.
- **Nano-Emulgel:**

- Made from nanoemulsions, where the droplet sizes are reduced to the nanometer range (1-100 nm).
- Incorporates similar gelling agents but benefits from the unique properties of nano emulsion.

2. Stability

- **Conventional Emulgel:**
 - More prone to phase separation or instability due to larger droplet sizes.
 - Requires careful formulation to maintain stability over time.
- **Nano-Emulgel:**
 - Generally more stable due to smaller droplet sizes that reduce gravitational separation and improve uniformity.
 - Enhanced stability against temperature changes and other environmental factors.

3. Skin Penetration

- **Conventional Emulgel:**
 - Provides decent skin penetration, but efficacy can vary based on the size of the droplets and the formulation.
- **Nano-Emulgel:**
 - Offers improved skin penetration and absorption due to the smaller droplet size, which enhances the permeability of active ingredients.
 - Can reach deeper layers of the skin more effectively.

4. Release Profile

- **Conventional Emulgel:**
 - Release of active ingredients can be slower and may lead to bursts of release.
- **Nano-Emulgel:**
 - Provides a controlled and sustained release of active ingredients, enhancing therapeutic efficacy and reducing side effects.

5. Sensory Attributes

- **Conventional Emulgel:**
 - May have a greasier feel depending on the oil phase and emulsifier used.



- The texture may vary, influencing user acceptance.
- **Nano-Emulgel:**
- Typically offers a lighter, less greasy texture, improving user experience and aesthetic appeal.
- Enhanced spreadability and absorption properties.

6. Formulation Challenges

- **Conventional Emulgel:**
- Easier to formulate with established techniques, but stability can be an issue.
- **Nano-Emulgel:**
- More complex to formulate due to the need for specialized equipment to produce and stabilize nanoemulsions.
- Requires careful selection of surfactants and stabilizers to avoid aggregation.

7. Applications

- Increasingly used in advanced drug delivery systems, targeting more specific therapeutic areas like transdermal drug delivery, due to improved efficacy.

- Nano-emulgels are composed of two main components: a thickening agent and a nano-emulsion, which can be either oil-in-water (o/w) or water-in-oil (w/o). The nano-emulsion contains nano-sized droplets of the dispersed phase, which can be either aqueous or oily.
- The gel matrix is generally created from polymers that can absorb liquid and swell, forming a stable structure. This design facilitates improved stability and regulated release of active ingredients.
- Different thickening agents, such as carbomers, xanthan gum, or hydroxypropyl methylcellulose, can be utilized, each providing unique characteristics to the formulation, such as viscosity, texture, and sensory feel. The selection of emulsion type and thickening agent will ultimately affect the product's efficacy, stability, and user experience.

Details of commonly used excipients in nano-emulgel formulations

Excipients	Type	Function
Gelling Agents		
Carbomers	Synthetic polymer	Thickening and stabilizing agent; forms gels upon neutralization.
Xanthan Gum	Natural polymer	Provides viscosity and stability.
Hydroxypropyl Methylcellulose (HPMC)	Semi-synthetic polymer	Gel-forming ability; enhances skin compatibility.
Surfactants		
Tween (Polysorbate 20/80)	Non-ionic surfactant	Stabilizes emulsions and enhances active ingredient solubility.
Span (Sorbiton Esters)	Non-ionic surfactant	Used in w/o emulsions; reduces

		interfacial tension.
Oils		
Mineral Oil	Hydrocarbon oil	Acts as an oily phase in emulsions.

Excipients	Type	Function
Essential Oils	Natural oils	Provide therapeutic effects and enhance fragrance.
Active Ingredients		
Antioxidants	Various	Protect formulations from oxidative degradation.
Skin Penetration Enhancers	Various	Improve the absorption of active ingredients through the skin.

Oils

The selection of oil in nano-emulgel formulation is critical, as it directly influences the emulsion's properties such as permeability, stability, and viscosity. Depending on the application—whether pharmaceutical or cosmetic—the oil phase can consist of natural or synthetic lipids, with the oil potentially serving as an active ingredient. The consistency of the lipid can range from liquid oils to high molecular weight solids, which impacts the overall formulation. Importantly, the hydrophobicity of the chosen oil is key to achieving a stable emulsion. Oils with poor hydrophobicity may enhance emulsification but can also compromise the solubility of lipophilic compounds. Therefore, careful consideration of the type and quantity of oil is essential in the development of nano-emulgels, as it lays the groundwork for an effective drug delivery system. Selecting the right oil not only ensures stability but also optimizes the release and absorption of active

ingredients, making it a fundamental aspect of formulation science. Natural oils are gaining attention for their medicinal properties, which can enhance the pharmacological efficacy of active ingredients in nano-emulgel formulations. For instance, oleic acid, commonly derived from both vegetable and animal sources, is a biodegradable and biocompatible omega-nine fatty acid known for its excellent solubilization capacity and ability to enhance percutaneous absorption. Its antioxidant properties contribute to cellular membrane integrity, repair cell damage, and stabilize formulations. Research by Arora et al. demonstrated that increasing oleic acid content from 3% to 6% significantly improved the permeability of ketoprofen in nano-emulgel preparations. Another noteworthy natural oil is emu oil, valued for its analgesic, antipruritic, and antioxidant properties. In a study by Jeengar and colleagues, a nano-emulgel formulation of curcumin with emu oil was developed to target



joint synovium diseases, resulting in enhanced permeability and superior pharmacological activity compared to pure curcumin. Additionally, emu oil is also popular in cosmetics for its moisturizing effects and high content of unsaturated fatty acids, including oleic acid, which further aids in drug penetration. These findings underscore the importance of selecting natural oils in nano-emulgel formulations, as they not only facilitate better drug delivery but also offer therapeutic benefits that can amplify the overall efficacy of the treatment.

Co-Surfactant System in emulsification

Co-surfactants play a crucial role in enhancing the efficacy of surfactants during the emulsification process of oil in water. They contribute to reducing interfacial tension and improving overall emulsification stability. By introducing flexibility to the interfacial film, co-surfactants facilitate the formation of transient negative interfacial tension, which is beneficial for creating stable emulsions.

Importance of Co-Surfactant Selection

The interplay between the surfactant and co-surfactant, alongside the partitioning behavior of the drug within immiscible phases, directly influences drug release from nano-emulgels. This makes the selection of co-surfactants as critical as that of surfactants. Commonly employed co-surfactants include:

- PEG-400
- Transcutol® HP
- Absolute Ethyl Alcohol
- Carbitol

Among these, alcohol-based co-surfactants are particularly favored due to their ability to partition between the oil and water phases, thereby enhancing miscibility.

Concentration Considerations

The concentration of co-surfactants must be carefully considered, as it can significantly impact the emulsification process. A combination of surfactants and co-surfactants with similar

Hydrophilic-Lipophilic Balance (HLB) values may lead to less stable emulsions. Non-ionic surfactants with varying HLB values are often more effective. Higher HLB surfactants tend to solubilize in the aqueous phase, while lower HLB surfactants preferentially solubilize in the non-aqueous phase, which enhances their interaction within the mixture.

Gelling Agents in Nano-Emulgels

Gelling agents are essential components in the formulation of nano-emulgels, contributing to the development of a cohesive three-dimensional network that enhances stability and consistency. By creating a colloidal mixture, these agents can form a weakly cohesive structure, either through physical or chemical cross-linking, which is crucial for topical applications.

Functions and Importance

Gelling agents influence several key parameters of the formulation, including:

- **Consistency:** Ensures the formulation maintains a desirable texture.
- **Rheological Properties:** Affects the flow and viscosity, which is vital for application.
- **Bio adhesive Properties:** Enhances adhesion to the skin, improving drug delivery.
- **Pharmacokinetics:** Influences the rate and extent of drug absorption.
- **Spreadability and Extrudability:** Affects how easily the formulation can be applied and dispensed.

Types of Gelling Agents

Gelling agents can be categorized based on their origin:

1. **Natural Gelling Agents:**
 - Composed of biopolymers and proteins.
 - Examples: Pectin, carrageenan, alginic acid, locust bean gum, and gelatin.
 - **Advantages:** Excellent biocompatibility and biodegradability.
 - **Limitations:** Susceptible to microbial degradation.



2. Semi-Synthetic Gelling Agents:

- Derivatives of natural polysaccharides.
- Examples: Hydroxypropyl cellulose, ethyl cellulose, sodium alginate.
- **Advantages:** Good biocompatibility and biodegradability; more stable than natural agents.
- **Response to Changes:** Better performance in varying conditions (pH, temperature).

3. Synthetic Gelling Agents:

- Chemically synthesized agents, with some FDA-approved.
- Examples: Carbomers and poloxamers.
- **Carbomers:** Polymerized acrylic acids that provide a range of rheological properties.
- **Poloxamers:** Triblock non-ionic copolymers, combining hydrophilic polyoxyethylene and a hydrophobic polypropylene chain.
- **Advantages:** Non-toxic, stable, and versatile, suitable for various applications.

Nano-Emulgel Preparation Methods

The preparation of nano-emulgels can vary significantly based on the sequence of mixing oil and aqueous phases. Various methods have been reported, each with distinct approaches and mechanisms. Here are some key techniques:

Mixing Techniques

1. Sequential Solubilization (Lupietal.w 2014)

- **Process:** The drug is solubilized in the oil phase, while the gelling agent is dissolved in the water phase separately. The oil phase is then gradually added to the aqueous gel phase under stirring, followed by homogenization to create an emulsion.
- **Conversion to Gel:** The sol form of the gelling agent in the emulsion can be transformed into a gel by adding a complexing agent or adjusting the pH to the desired level.

2. Two-Part Water Division (Dong et al., 2015)

- **Process:** The total water required for preparation is split into two parts. One part is used for pre-emulsion formation, while the other is utilized to prepare the gel. These components are mixed together under stirring.
 - **Advantages:** This method allows for better control over the emulsion and gel phases before combining them.
- ##### 3. 1:1 Mixing of Emulsion and Gel (Jeengar et al., 2016)
- **Process:** Emulsion and gel are prepared separately and then mixed in a 1:1 weight/weight ratio.
 - **Outcome:** This straightforward method allows for easy scaling and adjustments in the final formulation.

Energy Emulsification Techniques

Nano-emulgel formulation can be classified based on the emulsification techniques employed, which can be either high-energy or low-energy methods:

1. High-Energy Emulsification:

- **Description:** This approach uses mechanical devices to generate a significant disruptive force, resulting in size reduction of both phases.
- **Devices Used:** Microfluidizers, high-pressure homogenizers, and ultrasonication
- **Considerations:** While effective in producing nanosized emulsions (around 1 nm), this method can generate heat, which may compromise the stability of thermolabile drugs.

2. Low-Energy Emulsification:

- **Description:** This method utilizes spontaneous emulsification processes and typically requires less mechanical energy, which minimizes thermal effects on the formulation.

Permeability of Nano-Emulgel

In formulating emulsion-based gels, understanding the permeability and stability of the nano-emulgel is essential. Several process



parameters significantly influence the droplet size and overall stability of the formulation, which in turn drug delivery efficiency.

Key Considerations in Emulsion Preparation

1. Preparation Techniques:

- Various methods such as mechanical (rotor-stator), high-pressure homogenization, micro fluidization, and ultrasonic techniques are employed to create emulsions.
- Mechanical systems, like colloid mills, typically produce larger droplets (several microns), making them less desirable for nanoemulsion preparation.

2. Droplet Size Optimization:

- Achieving a droplet size below one micron is critical for enhancing the shelf life of emulsions by reducing creaming rates. Techniques like high-pressure homogenization and sonication are particularly effective in this regard.
- However, simply increasing the homogenization speed or duration is not sufficient. The optimal concentration of emulsifiers is necessary to prevent re-coalescence of droplets.

3. Role of Emulsifiers:

- The formulation's success often hinges on the right balance of emulsifier concentration combined with appropriate homogenization pressure and cycles. For instance, studies have shown that using an inadequate concentration of emulsifier can lead to larger globule sizes, as the newly formed surfaces may not be adequately stabilized.

4. Case Study: Sabna Kotta et al.

- This study highlighted the preparation of a nano emulsion using phase inversion and homogenization methods. By carefully adjusting the surfactant (gelucire 44/14) and co-surfactant (transcutol-HP) concentrations, they achieved smaller globule sizes and a favourable polydispersity index (PDI). This

emphasized the importance of optimizing emulsifier levels in conjunction with homogenization parameters.

5. Ultrasonication Approach:

- In a study by Mohammed S. et al., thymoquinone-loaded nano emulgels were developed using ultrasonication. Here, varying sonication times (3, 5, and 10 minutes) at a constant amplitude (40%) illustrated the effects on droplet size.
- Results indicated that decreased surfactant concentrations led to increased globular size after 10 minutes of ultrasonication. Conversely, higher surfactant concentrations facilitated the formation of smaller globules, showcasing the critical role of surfactant concentration in achieving desired nanoemulgel properties.

Permeability of Nano-Emulgel

The permeability of nano-emulgels through the skin is a critical factor in their effectiveness as topical delivery systems. The skin serves as a formidable barrier, primarily due to its outermost layer, the **stratum corneum**, which poses significant challenges for drug penetration.

Structure of the Skin

1. Stratum Corneum:

- Composed of keratinized cells, lipids, fatty acids, and cholesterol.
- Functions as a hydrophobic barrier, retaining moisture and preventing the entry of external agents.

2. Epidermis:

- Located beneath the stratum corneum, it provides additional protective layers.

3. Dermis and Subcutaneous Layer:

- These layers contain blood vessels and connective tissue, where drugs eventually need to reach systemic circulation.

Pathways for Drug Penetration

When a drug is released from the gel matrix of a nano-emulgel, it must navigate through the skin's



layers. The main pathways for drug penetration include:

1. **Transcellular Transport (Intracellular Transport):**

- This pathway involves the movement of drug molecules directly through the cells of the stratum corneum.
- The process is driven by concentration gradients, allowing drugs to diffuse across the cellular membranes.

2. **Paracellular Transport:**

- Here, the drug passes through the intercellular spaces between skin cells.
- This pathway is influenced by the tight junctions between cells, which can restrict or facilitate the movement of drug molecules based on their size and charge.

3. **Transappendageal Transport:**

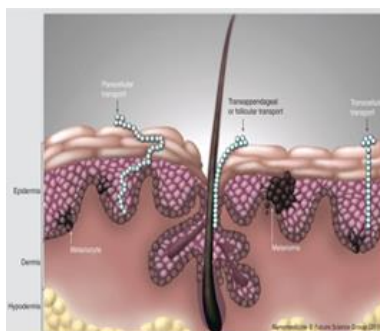
- Although this pathway exists through hair follicles and glandular ducts, its contribution to overall drug penetration is minimal due to the small surface area these appendages occupy.

Role of Nano-Size Droplets

The small diameter of nano-sized droplets enhances their ability to traverse the skin barrier. Their reduced size allows for:

- **Increased Surface Area:** Greater interaction with the skin, facilitating higher absorption rates.

Improved Permeation: Smaller particles can more easily penetrate both the stratum corneum and deeper layers of the skin.



Characterization Studies of Nano-Emulgel

Characterization of nano-emulgels is essential to ensure their quality, consistency, and efficacy across different batches. The evaluation involves a range of tests that assess both physical and chemical properties, as well as performance characteristics relevant to their application in drug delivery.

Essential Characterization Tests

1. **General Pharmaceutical Tests (USP Guidelines):**

- **Description:** Physical appearance and consistency of the formulation.
- **Identification:** Confirmation of the active pharmaceutical ingredient (API).
- **Assay:** Measurement of the API concentration.

- **Impurities:** Detection of any contaminants or degradation products.

2. **Specific Tests for Topical Dosage Forms:**

- **Uniformity of Dosage Units:** Ensures each dose contains the intended amount of API.
- **Water Content:** Measurement of moisture, which can affect stability.
- **Microbial Limits:** Assessment of microbial contamination to ensure safety.
- **Antimicrobial and Antioxidant Content:** Evaluates efficacy and stability.
- **pH:** Critical for skin compatibility and stability.
- **Particle Size and Polydispersity Index (PDI):** Essential for understanding the distribution and uniformity of nanosized droplets.

- **Sterility:** Verification that the product is free from viable microorganisms.
- **Polymorphic Nature of API:** Analysis of the crystalline form of the API, which can influence solubility and stability.
- 3. **Additional Characterization Parameters for Nano emulgels:**
 - **Zeta Potential:** Indicates the stability of the nano-emulsion; a higher absolute value suggests better stability against coalescence.
 - **Droplet Size:** Smaller droplet sizes generally lead to improved permeability and stability.
 - **In-Vitro Release Studies:** Assessment of the drug release profile over time to determine the formulation's release characteristics.
 - **Spreadability:** Evaluates how easily the nano-emulgel can be spread on the skin, affecting application and absorption.
 - **Bio-Adhesive Tests:** Measures the formulation's ability to adhere to skin, which can enhance drug delivery.
 - **Skin Irritation Tests:** Assess potential irritation or adverse reactions upon topical application.
 - **Ex-Vivo Permeability Studies:** Evaluate how effectively the formulation penetrates through skin layers.
 - **In-Vivo Bioavailability:** Determines the overall effectiveness of the formulation in delivering the drug systemically.
- Adjacent to this stern layer is a **diffuse layer** of loosely bound ions.
- Together, these layers form the **electrical double layer**, which is crucial for understanding particle interactions.
- 2. **Slipping Plane:**
 - The **zeta potential** is defined as the electrostatic potential at the boundary (the "slipping plane") between the diffuse layer of ions moving with the particle and those remaining in the bulk dispersant.
 - This potential reflects the net charge of the particles and indicates how they will interact with each other in a dispersion.

Importance of Zeta Potential

- **Stability Indicator:**

- A higher zeta potential signifies greater electrostatic repulsion between particles, which enhances the stability of the formulation. High zeta potential values help prevent particle aggregation or coalescence in emulsions.

- **Batch-to-Batch Consistency:**

- Measuring zeta potential allows for the assessment of consistency between different batches of nano-emulgel, ensuring uniformity in performance and stability.

- **Modification of Surface Charge:**

- The zeta potential can be altered by using surface charge modifiers. For instance, adding a negatively charged surfactant will result in a negative zeta potential, while a positively charged modifier will yield a positive zeta potential.

Role of Surfactants

- **Stabilization Mechanism:**

- Surfactants, whether anionic or cationic, play a crucial role in enhancing the stability of emulsions. By modifying the surface charge, surfactants can significantly impact the zeta potential and, consequently, the formulation's stability.

Zeta Potential

Zeta potential is a critical parameter in characterizing the stability of colloidal systems, including nano-emulgels. It provides insights into the electrostatic interactions between particles in a dispersion, influencing their behaviour and stability.

Understanding Zeta Potential

1. Electrical Double Layer:

- Particles in a solution typically have an ionic layer on their surface known as the **stern layer**.



Measurement Techniques

Zeta potential can be measured using various instruments, including:

- **ZC-2000 (Zeecom-2000, Microtec Co. Ltd., Chiba, Japan)**
- **Malvern Nanosizer/Zetasizer® nano-ZS ZEN 3600 (Malvern Instruments, Westborough, MA, USA)**

These devices provide precise measurements of zeta potential, enabling formulators to optimize formulations for improved stability and performance.

Spreadability Testing

Spreadability is a crucial property for topical dosage forms, as it ensures uniform application and effective delivery of the drug. The spreadability of nano-emulgels can significantly influence their therapeutic efficacy, and understanding how to measure this property is essential for formulation development.

Importance of Spreadability

- **Uniform Dose Delivery:** Good spreadability ensures that the product can be evenly distributed over the skin, allowing for consistent dosing and improved absorption.
- **Viscosity Influence:** The viscosity of the nano emulgel plays a vital role in its spreadability. Higher viscosity may hinder spreadability, while lower viscosity may enhance it.

Measurement Methods

While no standardized method exists for measuring spreadability, several techniques are commonly used to approximate this property:

1. **Parallel-Plate Method (Slip and Drag Method):**
 - **Setup:** This widely employed technique uses two glass slides of equal length. One slide is fixed, while the other is movable and connected to a pulley.
 - **Procedure:**

- The nano-emulgel is placed on the stationary glass slide.
- The upper slide is then pressed down to squeeze the emulgel, ensuring even spreading and removal of air bubbles.
- Weights are gradually added to the pulley until the upper slide slips off the lower slide.
- The time taken for this slipping event is recorded.
- **Calculation:** The spreadability (S) is calculated using the formula:
$$S = \frac{M \times L}{T}$$
Where:
 - S = Spreadability
 - M = Weight applied (force)
 - L = Distance between the slides
 - T = Time taken for the upper slide to slip off

2. Human Subject Assessment:

- This qualitative method involves applying the formulation on the skin and subjectively evaluating its spreadability based on user experience.
- While not as precise as instrumental methods, it provides valuable insights into the practical performance of the product.

In-Vitro Release Test (IVRT)

The In-Vitro Release Test (IVRT) is a critical evaluation method for assessing the drug release characteristics of semi-solid dosage forms, such as nano-emulgels. It provides essential insights into the efficacy and safety of the active pharmaceutical ingredient (API) by simulating the drug release process under controlled conditions.

Importance of IVRT

- **Quality Assessment:** IVRT serves as a key tool for determining the quality and performance of topical formulations.
- **Predictive Value:** It helps predict how the formulation will behave in vivo, aiding in the development of effective drug delivery systems.



Testing Methodology

According to FDA guidelines, IVRT for semi-solid dosage forms can be conducted using two primary setups: the **vertical diffusion cell** and the **immersion cell**.

1. Vertical Diffusion Cell:

○ Components:

- **Receptor Chamber:** Contains the receptor medium (buffer or hydro-alcoholic solution).
- **Donor Chamber:** Holds the sample of the dosage form.
- **Receptor Membrane:** Separates the donor and receptor chambers; it mimics skin permeability and is selected based on effective pore size and inertness toward the API.

○ Procedure:

- The receptor medium is prepared based on the API's solubility and stability.
- If necessary, the receptor membrane is saturated with the release media.
- The system is maintained at a temperature of approximately $32\text{ }^{\circ}\text{C} \pm 1\text{ }^{\circ}\text{C}$ for topical products or $37\text{ }^{\circ}\text{C} \pm 1\text{ }^{\circ}\text{C}$ for products intended for mucosal membranes.
- A Teflon-coated magnetic stirrer is used to agitate the receptor media, ensuring consistent mixing.

2. Immersion Cell:

○ Setup:

- The immersion cell acts as a reservoir and is covered with a membrane that is sealed to prevent leakage.
- The membrane contacts the dosage form below and is in contact with the release media above.

○ Procedure:

- The immersion cell is placed in a flat-bottomed dissolution vessel, usually containing **150–200 mL** of release media.
- A mini spin-paddle is utilized for stirring or agitating the media to ensure homogeneity.

Considerations for IVRT

- **Media Selection:** The choice of receptor media should reflect the intended use and solubility characteristics of the API to maintain sink conditions.
- **Temperature Control:** Maintaining the appropriate temperature is crucial for mimicking physiological conditions and ensuring accurate results.

Membrane Selection: A suitable skin-like membrane is vital for effective simulation of drug release.

Grade	Description	Clinical Implications
0	No irritation	Safe for use; no need for formulation changes.
1	Very slight irritation (erythema, slight edema)	Minimal concern; may require monitoring in sensitive populations.
2	Mild irritation (redness and swelling)	Consider formulation adjustments; patient feedback encouraged.
3	Moderate irritation (intense erythema and edema)	Significant concern; potential need for reformulation or ingredient replacement.
4	Severe irritation (extensive damage, ulceration)	High risk; immediate withdrawal of product recommended.

Clinical Implications of Skin Irritation Grading

Aspect	Details
Formulation Safety	Higher grades indicate safety issues; changes may be necessary.

Regulatory Compliance	Essential for meeting safety standards in regulatory submissions.
Patient Tolerance	Lower grades suggest better tolerance, improving adherence.



Product Development	Guides iterative improvements in formulation based on irritation responses.
Clinical Trials	Provides critical safety data; influences trial design and endpoints.
Post-Marketing Surveillance	Ongoing monitoring helps identify long-term safety issues.

Current and Future Prospects of Nano emulgel

Delivering hydrophobic drugs effectively remains a significant challenge in formulation development due to their low solubility, which often leads to poor bioavailability. Traditional topical formulations, such as creams, ointments, and lotions, offer good emollient properties but are hindered by slow drug release kinetics because of their hydrophobic bases, such as petrolatum, beeswax, and vegetable oils. These bases restrict the incorporation of water, limiting the overall effectiveness of the formulation. In contrast, aqueous-based formulations like gels facilitate better drug release by providing a suitable aqueous environment for the active pharmaceutical ingredients (APIs). By combining hydrophobic APIs with oily bases, emulgels can be created, which are then subjected to nano ionization to produce nano emulgels. These nano emulgels exhibit superior characteristics, including thermodynamic stability, enhanced permeation, and sustained release, making them an attractive dosage form. The market for nano emulgels is expanding, with several products already commercialized and numerous patents filed, indicating significant progress in this area. Ongoing research is likely to advance the development of nano emulgels as a viable delivery system, particularly for drugs that have been side lined due to poor bioavailability or therapeutic inefficacy. Despite the advantages of nano emulgels, challenges remain, particularly in manufacturing and commercialization. Current production techniques may not be commercially

viable, which could limit widespread adoption. However, as technology progresses, more efficient and cost-effective manufacturing methods are expected to emerge, paving the way for increased production and application of nano emulgel.

Schematic representation for the preparation of nano-emulgel by (A) adding Oil (oil + drug) phase to aqueous (water + gelling agent) phase (B) adding nano-emulsion to aqueous (water + gelling agent) phase.

Vehicle Properties

The formulation of an emulgel relies on the selection of an appropriate vehicle, which should possess the following properties:

- **Effective Drug Deposition:** The vehicle should efficiently deposit the drug on the skin, ensuring even distribution across the application area.
- **Drug Release:** It must facilitate the release of the drug so that it can migrate freely to the target site.
- **Targeted Delivery:** The vehicle should deliver the drug directly to the intended site of action, enhancing localized effects.
- **Sustained Therapeutic Levels:** It should maintain therapeutic drug levels in the target tissue for a sufficient duration to exert a pharmacological effect.
- **Anatomic Suitability:** The formulation needs to be appropriately tailored for the specific anatomic site being treated.
- **Cosmetic Acceptability:** The emulgel must be cosmetically appealing to patients, ensuring comfort and compliance during use.

Due to the efficiency of the epidermal barrier, the amount of topical drug that penetrates through the stratum corneum is typically low. The rate and extent of absorption can vary significantly based on the characteristics of the vehicle as well as the nature of the active ingredient.

Aqueous Phase



The aqueous phase is a critical component of the emulgel formulation. Commonly used agents in this phase include:

- **Water:** Acts as the primary solvent and provides the aqueous environment necessary for drug release.
- **Alcohols:** Such as ethanol or isopropyl alcohol, which can enhance skin permeability and aid in the solubilization of hydrophobic drugs.
- **Electrolytes:** For instance, sodium chloride may be added to adjust osmotic pressure or enhance stability.

Formulation of Emulgel

Oils

Mineral oils are commonly used in external emulsions, either alone or in combination with soft or hard paraffin. These oils serve as a drug delivery system and provide occlusive properties, enhancing skin sensation. In oral preparations, mineral and castor oils are often utilized for their laxative effects. While not biodegradable, these oils can be stable options, and vegetable oils from sources like Arachis, cottonseed, and maize are also popular as dietary supplements.

Emulsifiers

Emulsifying agents are crucial in the manufacturing process of emulsions, helping to enhance stability throughout the product's shelf life, which can range from days to years. Common emulsifiers include:

- **Polyethylene Glycol 40 Stearate**
- **Polyethylene Sorbiton (Span 80)**
- **Sorbiton Mono-Oleate**
- **Sodium Stearate**
- **Stearic Acid**
- **Polysorbate 80 (Tween 80)**

These emulsifiers facilitate the formation and maintenance of stable emulsions.

Gelling Agents

Gelling agents increase the viscosity of the dosage form and serve as thickening agents. Common gelling agents used in emulgels include:

Gelling Agent	Quantity	Dosage Form
Carbopol-934	0.5% - 2%	Emulgel
Carbopol-940	0.5% - 2%	Emulgel
HPMC-2910	2.5%	Emulgel
HPMC	3.5%	Gel
Sodium CMC	1%	Gel

Penetration Enhancers

Vehicles may include penetration enhancers that temporarily disrupt lipid channels between corneocytes, aiding drug distribution and improving skin penetration.

Properties of Penetration Enhancers:

1. Non-toxic, non-irritating, and non-allergenic.
2. Rapid acting, with predictable and reproducible effects.
3. No pharmacological activity within the body (i.e., do not bind to receptor sites).

Mechanisms of Action: Penetration enhancers can work through three main mechanisms:

1. Disruption of the ordered structure of stratum corneum lipids.
2. Interaction with intercellular proteins.
3. Improved partitioning of the drug, co enhancer, or solvent into the stratum corneum.

Preparation of Emulgels

Step 1: Formulation of O/W or W/O Emulsions

The first step involves dissolving oil-soluble substances in the oil phase (e.g., dissolving Span 20 in liquid paraffin) and water-soluble substances in the aqueous phase (e.g., Tween 80 in purified water). The two phases are mixed under turbulent conditions to ensure dispersion into droplets. In laboratory settings, mechanical stirrers are used, while industrial processes may employ homogenizers, ultrasonication- or colloid mills.

Step 2: Formulation of Gel Base

Water-soluble excipients are dissolved in the aqueous vehicle using mechanical stirring. To prevent aggregation, hydrophilic polymers are slowly added to the



stirred mixture. Stirring continues until the polymer is fully dissolved, ensuring the pH remains within the desired range. Care should be taken to avoid excessive stirring, as this can entrap air in the gel.

Step-by-Step Preparation of Emulgels

Step 3: Addition of Emulsion to Gel Base In this step, the emulsion phase is gradually blended into the gel base at a ratio of approximately 1:1 to create the emulgel. This blending should be done steadily to ensure uniform dispersion.

General Steps in the Preparation of Emulgels

1. Formulation of O/W or W/O Emulsions

- Dissolve oil-soluble substances in the oil phase and water-soluble substances in the aqueous phase.
- Mix both phases under turbulent conditions using mechanical stirrers or industrial equipment.

2. Formulation of Gel Base

- Dissolve water-soluble excipients in the aqueous vehicle with mechanical stirring.
- Slowly add hydrophilic polymers to prevent aggregation, ensuring complete dissolution.

3. Addition of Emulsion to Gel Base

- Combine the emulsion with the gel base in a 1:1 ratio, blending steadily to create a uniform emulgel.

Evaluation of Emulgels

1. Fourier Transform Infrared Spectroscopy (FTIR)

- Used to assess the compatibility of excipients and stability of the drug in its solid state.

2. Physical Examination

- Visually inspect the emulgel for color, homogeneity, consistency, and phase separation.

3. Determination of pH

- Measure pH using a digital pH meter after rinsing the electrode with distilled water.

4. Measurement of Viscosity

- Use a Brookfield Viscometer to assess viscosity, allowing the sample to settle for 30 minutes before measurement.

5. Spreadability

- Evaluate using two glass slides: apply the emulgel between the slides and measure the time taken for the upper slide to detach under a specified weight.

6. Globule Size and Distribution

- Determine using Malvern zeta sizing, where a sample is dissolved in filtered water and analyzed for globule size and distribution.

7. Swelling Index

- Measure by immersing the emulgel in a 0.1 N NaOH solution, then weighing at specified intervals.

8. In Vitro Drug Release Study

- Conduct using an egg membrane in diffusion cells, stirring with a magnetic stirrer and sampling at intervals for analysis.

9. Microbiological Assay

- Utilize the ditch plate method to evaluate bacteriostatic or fungistatic activity against relevant microorganisms.

10. Skin Irritation Test

- Apply the emulgel to the skin of rabbits and assess for any irritation after a specified exposure period.

11. Stability Studies

Pack the emulgels in aluminium collapsible tubes and conduct stability tests under various temperature and humidity conditions over three months.

Packaging of Emulgels

Emulgels are typically packaged in:

- **Membrane-Sealed Aluminium Tubes:** Coated with a phenoxy-epoxy lacquer and closed with a propylene screw cap.

Aluminium Laminated Tubes: Sealed with a moulded cap for enhanced protection.

Marketed Formulations



Sr. No	Brand Name	Active Ingredient	Manufacturer	Uses
1	Voltarol	Diclofenac Diethyl ammonium Salt	Novartis	Anti-inflammatory
2	Miconaz Hemulgel	Miconazole Nitrate, Hydrocortisone	Medical Union Pharmaceuticals	Topical corticosteroid
3	Denacine Emulgel	Clindamycin Phosphate	Beit Jala Pharmaceutical Company	Anti-acne
4	Diclou	Diclofenac Diethylamine	Medpharma	Anti-inflammatory
5	Cataflam Emulgel	Diclofenac Potassium	Novartis	Anti-inflammatory

CONCLUSION

Emulgels represent an innovative formulation technique that combines the advantages of gels and emulsions, making them an efficient and convenient drug delivery system. Their non-greasy nature and absence of excess oily bases allow for a gel-like consistency, which facilitates excellent drug release compared to traditional topical formulations. Due to improved patient compliance, the topical drug delivery system will be utilised extensively. The spreadability, adhesion, viscosity, and extrusion advantages of emulgel will make them an increasingly popular drug delivery method. In the future, these physical and physico-chemical properties will be utilized to deliver a greater number of topical medications, such as emulgel. In summary, emulgels represent a significant advancement in topical drug delivery systems, merging the advantages of both emulsions and gels to enhance the stability, release, and overall efficacy of active pharmaceutical ingredients. Comprehensive studies, including microbiological assays, skin irritation tests, and stability evaluations, are crucial to ensure that these formulations are safe, effective, and suitable for consumer use. By rigorously assessing the physical, chemical, and microbiological properties of emulgels, formulators can optimize their designs to meet regulatory standards and consumer expectations.

As the pharmaceutical industry continues to innovate, emulgels stand out as a promising solution for improving therapeutic outcomes in dermatology and other fields. This underscores the importance of ongoing research and development to fully realize the potential of emulgels in enhancing drug delivery and patient care.

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