



## AN REVIEW ON TOPICAL DELIVERY SYSTEM

**Kardile Pooja\*, Snehal lad, Dr.Sanjay Garje , Dr.Gaffar. Sayyed**  
SAJVPM'S College Of Pharmaceutical Science And Research Centre, Kada ( Beed ), Maharashtra, India

\*Corresponding Author; Kardile Pooja

### ABSTRACT

Topical drug delivery (TDD) is a method of administering medication that produces a localized effect to treat skin conditions such as eczema by allowing the topical formulation to be dispersed throughout the skin upon application. Topical medication formulations fall into four categories: corticosteroids, antibiotics, antiseptics, and antifungals. The drug's skin-based metabolism and diffusion are part of the topical delivery method. In 3000 BCE, topical medication delivery became the first method of drug delivery to people in ancient Egypt and Babylonia. Topical treatments such as ointments and potions were applied topically in these ancient cities because topical medication distribution involves passing through several layers of skin and pharmacokinetics, factors including cutaneous illnesses reduce the bioavailability of the topical medications. Topical drug delivery is improving as a result of the widespread usage of topical medications. Through the application of chemical and physical agents, these developments improve the delivery of topical drugs to the skin. To improve topical drug absorption for chemical agents, carriers such as liposomes and nanotechnologies are employed. However, physical agents such as microneedles are a further strategy for improving absorption. The efficiency of topical formulation is governed by elements such as pH, lipophilicity, and drug molecule size, in addition to the use of carriers.

**KEYWORDS:** Hypodermis, dermis, depilatory, exfoliating, antiperspirant, abrasive, antipruritic

### INTRODUCTION

Pharmaceutical formulation scientists are now exploring non-oral/parenteral methods for the efficient and effective administration of drugs to the target site, thanks to advancements in pharmaceutical technologies. The optimal distribution of treatments at the site of action within the allotted time frame is included in effective medication administration. For the purpose of treating localized illnesses, the topical delivery system is a technique in which the formulation is given topically to locations including the skin, eyes, nose, and vagina. When a medicine is applied topically, it avoids the first pass metabolism in the liver, changes in gastric pH, and fluctuations in plasma levels, which are often associated with oral drug administration.

The other advantages associated with the topical drug delivery system include the following

- ❖ Patient compliance and acceptance
- ❖ simplicity and ease of application
- ❖ painless and noninvasive approach
- ❖ enhanced drug absorption
- ❖ improved physiological and pharmacological response
- ❖ minimal systemic toxicity
- ❖ and medication exposure to non-infectious tissue/sites are all important considerations.

Developing a topical delivery system is a difficult undertaking that necessitates careful consideration of both the active ingredient and the delivery method, as the obstacles connected to these routes may restrict the drug's availability at the site of effectiveness

The primary barrier preventing foreign particles from penetrating the skin is the stratum corneum. Within minutes of topical administration, 95% of medicines are removed from the surface of the eye. Conventional vaginal compositions' low efficacy stems from the efficaciousness of traditional vaginal formulations is restricted due to their poor distribution over the vaginal tissues and brief residence period. These drawbacks highlight the necessity for in-depth study to create novel and creative delivery systems by altering the constituents of the formulation or the ways in which they are administered. Figure 1 shows the several formulations that are presently being investigated for topical medication delivery. The most current research on topical medication delivery methods The United States (US) and World Intellectual Property Organization (WIPO) registered patents issued between 2012 and 2015 were found using the Espacenet and PatentScope databases of the WIPO. These patents revealed innovative topical delivery formulation strategies. An attempt has been made to review all of the new formulation technologies with illustrative examples in this article.

### Topical drug delivery system

The skin, vagina, eyes, and nose are the main routes for topical delivery that have been extensively studied. This section offers a basic overview of the physiology of diverse pathways, the protective barriers that go along with them, and the most current patent applications and approvals for neoteric compositions applied topically.



### Factors Affect Topical Absorption

Only the topical drug's physicochemical characteristics have an impact on how many molecules of the medication are transported to the skin. The medication molecule's weight is the first consideration. The rate at which a medicine diffuses and absorbs into the skin increases with decreasing drug molecular weight or particle size. Given how lipophilic the three absorption channels are, the second element is the lipophilicity of the drug molecules. In contrast to hydrophilic drug molecules, it is easier for this type of medicine to be absorbed due to its increased lipophilicity. The skin's pH level is the third parameter. Since the skin's layers have a basic pH, basic topicals will absorb more readily than acidic ones topical medications. These elements are essential in determining the topical drug delivery system's permeability

The factors that affect the topical absorption are as follows

#### 1. Physiological factors:

- ❖ Lipid content.
- ❖ Density of hair follicles.
- ❖ Density of sweat glands.
- ❖ Skin pH.
- ❖ Blood flow.
- ❖ Hydration of skin.
- ❖ Inflammation of skin.

#### 2. Physicochemical factors.

- ❖ Molecular weight
- ❖ Partition coefficient.

### Purpose of Topical Preparation

The intended objective must be taken into account while creating a topical medication that is both effective and efficient. This immediately relates to the intended outcome of the preparation as well as the site of action.

Topical treatments can be applied to:

- i) Surface effects: antibacterial (lower risk of infection), cosmetic (improvement of look), protective (avoid moisture loss, sunscreen), and cleansing (removal of dirt and germs).
- ii) Effects on the stratum corneum: keratolytic (a skin sloughing that helps treat psoriasis), hydrating, and protective (such as sunscreens that penetrate this layer).
- iii) Effects on the epidermis and dermis that are viable: a number of medication classes, including anti-inflammatory, anesthetic, antipruritic, and antihistamine ones, may permeate these layers. Drugs find it challenging to enter the stratum corneum, yet once they have the ability to permeate into the bloodstream in the dermis. Creating a medication that has a localized effect without being absorbed by the bloodstream is challenging.
- iv) Systemic effects: Some medications, including estradiol, nitroglycerin, scopolamine, and clonidine, have been designed to have systemic effects.
- v) Appendage effects: Certain drug classes (depilatory, exfoliating, antibacterial, and antiperspirant) are designed to act on certain areas of the skin

### Skin Drug Delivery

The skin, which has a surface area of 1.5 to 2 m<sup>2</sup>, is the biggest organ in the human body and serves as the most intricate barrier separating the biological system from the outside world. It is a

three-layered structure with an outer layer that is between 50 and 150 μm thick (the biological barrier), 250 μm the innermost subcutaneous fatty tissue (a mechanical cushion) and the thick dermis (a heat barrier) The epidermal region is made up of the stratum corneum's superficial layers, whose distinct cellular architecture acts as a barrier to the passage of molecules larger than 500 Da, offering physical defense against microbial invasion.

Millions of people suffer from skin problems every day. The conditions that fall under this category are classified as autoimmune (scleroderma, psoriasis), fungal (sporotrichosis, chromomycosis, blastomycosis), viral (herpes simplex virus, eczema), and bacterial (impetigo, cellulitis). Drugs that are applied topically to the skin's surface are always being researched for the local treatment of various illnesses. The majority of exogenous compounds (drugs/active moiety) exhibit resistance to permeability, which poses a significant difficulty in the design of topical drug delivery systems. Furthermore, creating an effective topical administration method is challenging due to changes in the skin's barrier qualities and permeability associated with the disease.

### Skin-Related Bases

Topical treatments intended for local or systemic effects are typically categorized as:

Solids – Dusting powder

Semi-solids – Creams, Gel, Ointments, Paste and other

Liquids – Solution, Emulsion, Liniments, Suspension, Soaps, Shakes, Collidons, Lotion, Paints and other.

These semi-solid formulations are more promising than solid and liquid ones because of their ability to adhere to the application surface for a suitable amount of time before wearing off.

Pharmaceutical semi-solid formulations consist of gel, cream emulsions, pastes, ointments, and stiff forms.

### Benefits of Topical Medication Delivery Methods

1. Avoiding the metabolism of the first pass.
2. Practical and simple to use.
3. Avoidance of the dangers and difficulties associated with intravenous therapy as well as various absorption conditions such as changes in pH
4. The presence of enzymes and the duration of gastric emptying.
5. Terminating the drugs is simple when necessary.
6. More carefully deliver the medication to a targeted area.
7. Avoiding the incompatibility with the stomach.
8. Enabling the use of medications having a brief biological half-life and a limited window of therapeutic use.
9. Increased adherence from patients.
10. Assist with appropriate self-medication.
11. Drug input continuously allows for the achievement of efficacy with a reduced total daily dose of the medication.

12. Prevents medication level fluctuations as well as intra- and inter-patient variability.
13. A quite large area of application in comparison with buccal cavity. Ability to deliver drugs more selectively to a specific site

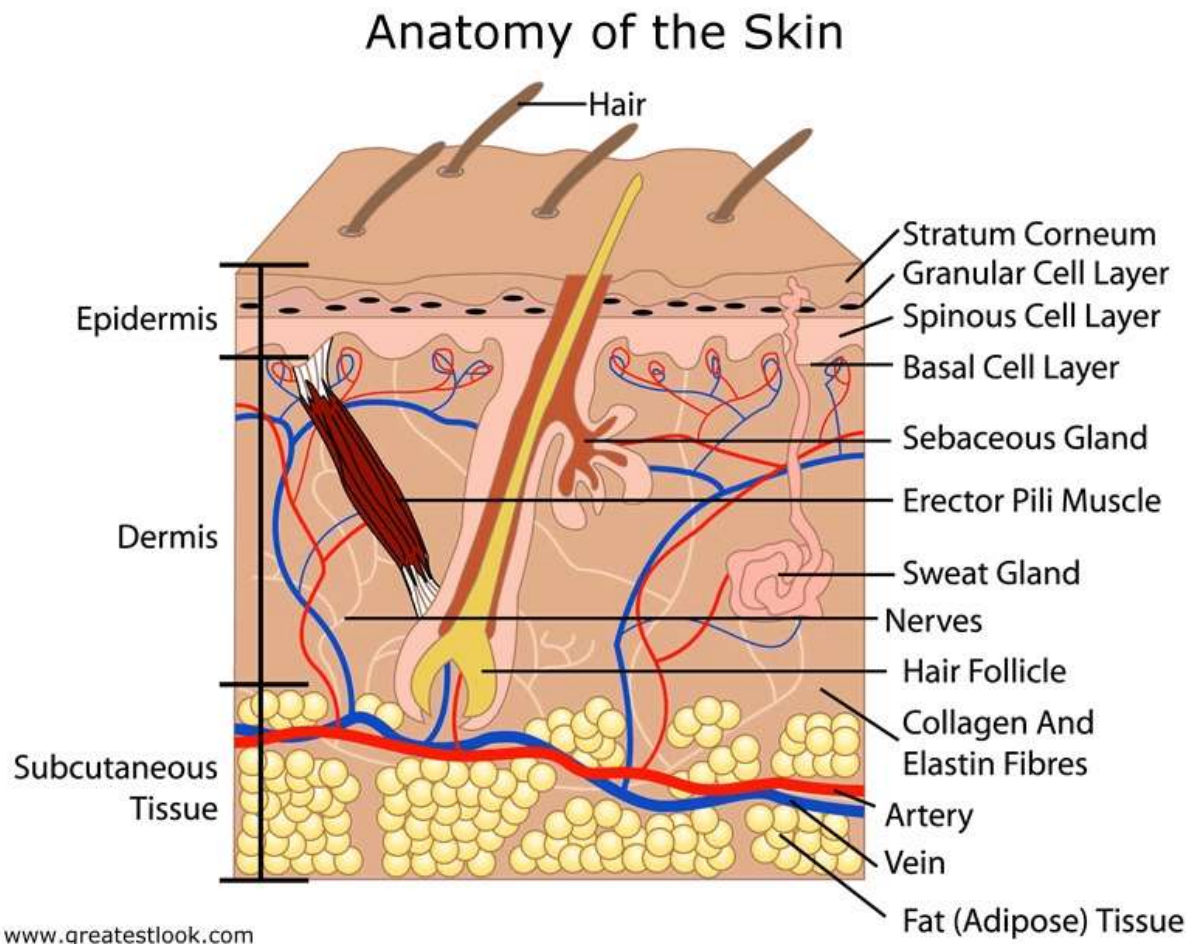
4. likelihood of allergic responses.  
Can only be applied to medications whose actions depend on extremely low plasma concentrations
5. Drugs that cause skin irritation or hypersensitivity should not be taken via this route

#### Topical medication Delivery Techniques' Drawbacks

1. The medication or its ingredients may cause dermatitis or skin irritation.
2. Certain medications don't pass through the skin well.
3. Greater particle size drugs are more difficult to absorb via the skin.

#### Skin Anatomy

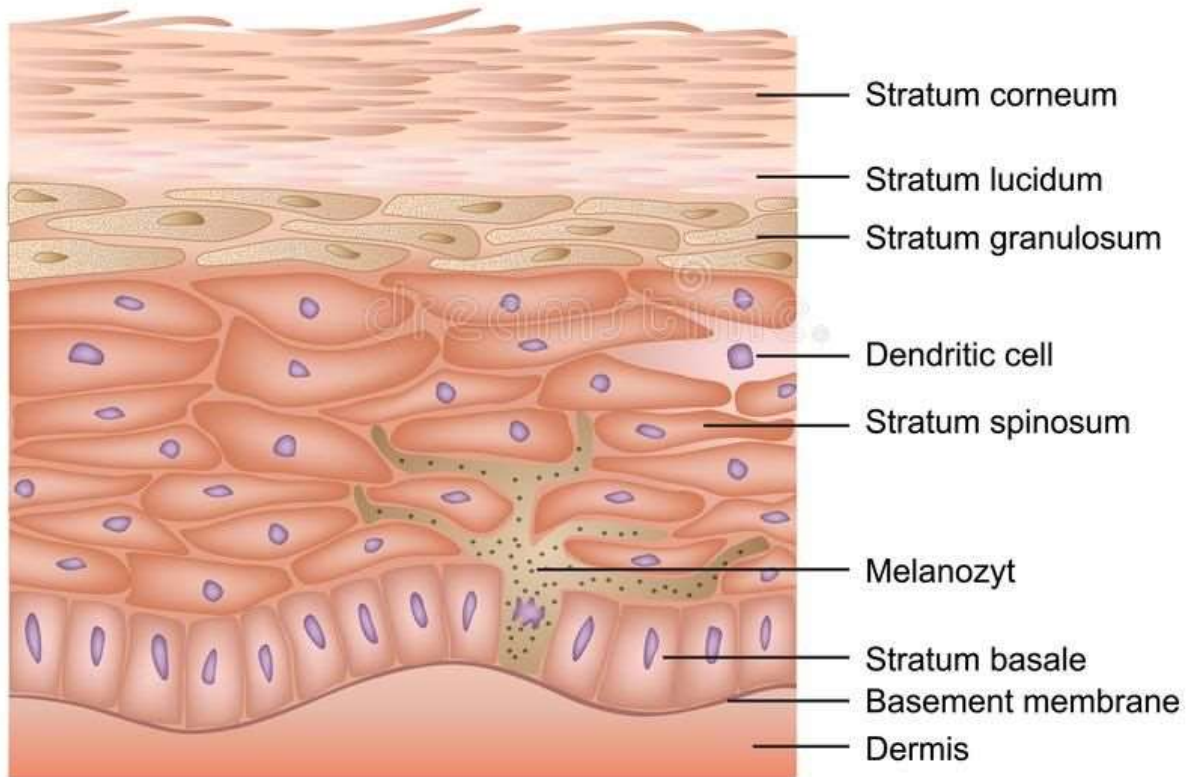
The human skin is composed of three interdependent tissues: The cellular, stratified layer known as the "epidermis" lies beneath the dermis of connective tissues the hypodermis.





❖ Epidermis

# Structure of the Epidermis

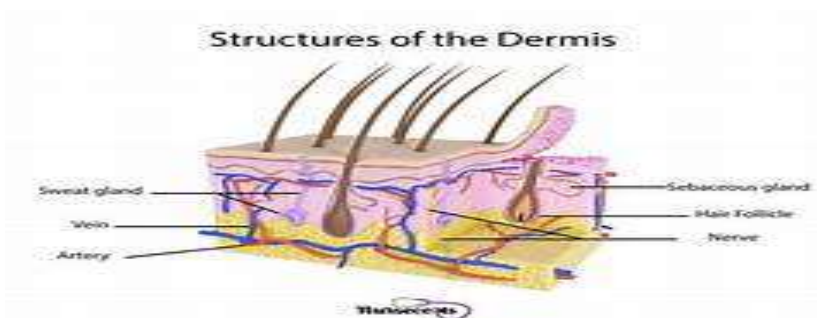


The epidermis of the skin is formed by stratified epithelium, which is made up of 5 layers:

1. Stratum corneum.
2. Stratum lucidum
3. Stratum granulosum
4. Stratum spinosum and
5. Stratum germinativum

The absence of blood vessels in the epidermis is its most significant characteristic. The dermal capillaries supply the nourishment. The uppermost layer of skin is called the epidermis, and it is a stratified, squamous, keratinizing epithelium. The keratinocyte count, which determines the skin's barrier properties, is greater than 90%.

❖ Dermis

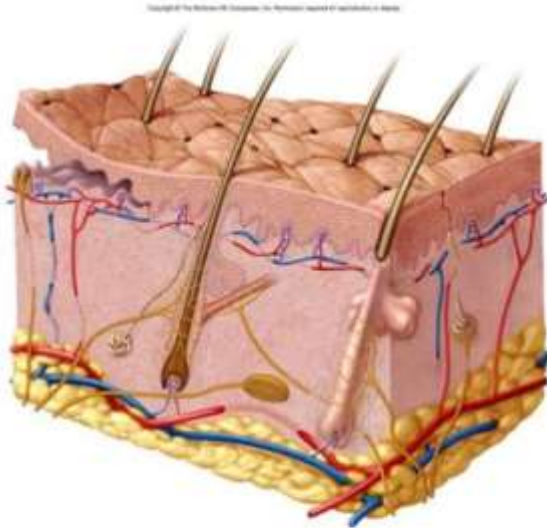


Its flexibility and strength are derived mostly from a thick layer of fibrous and elastic tissue called the dermis, which is composed primarily of collagen, elastin, and fibrillin. Blood veins, sweat glands, oil glands, nerve endings, and hair follicles

are all found in the dermis. The dermis is a vascularized connective tissue rich in collagen that contains mucopolysaccharides, also referred to as the ground material.

❖ Hypodermis

## § Hypodermis



1. Other names--  
Subcutaneous tissue;  
superficial fascia
2. Mostly adipose tissue;  
Uniformly distributed?; **8%  
thicker in women**
3. Functions
  - energy reservoir
  - thermal insulation
4. Hypodermic injections  
(to subcutaneous tissue)
  - highly vascular; **absorb  
drugs easily**

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The epidermis is the skin's innermost layer. It is the layer of tissue that comes into contact with the body's underlying tissues, including the muscles and bones. Although they originate in the dermis, sweat glands, sebaceous glands, and hair follicles are encased in the epidermis.

A diluted salt solution is released onto the skin's surface via sweat glands. Skin cools down as a result of this diluted salt solution evaporating, which is crucial for controlling body and skin temperature. The body is covered in sweat glands. The amount of heat producing skeletal muscle activity, the temperature of the surrounding environment, and a variety of emotional elements all affect how many dilutions (sweat) are created. Sebum is an oily liquid that is secreted into hair follicles and then lands on the epidermis. Sebum prevents drying out of the skin and hair and offers a waterproof layer

### Evaluation of Ointments

Penetration

EVALUATION OF TOPICAL DOSAGE

FORM

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There have been some very basic experiments suggested for determining the penetration. For a specified amount of time, specific skin areas are treated with weighed volumes of the ointments. After that, the ointment that hasn't been absorbed is removed from the skin and weighed. Roughly speaking, the difference between the two weights indicates the amount absorbed.

Irritant Effect

Generally speaking, no ointment should irritate the skin, mucous membranes, or the skin itself. The skin of rats or the eyes and skin of rabbits can be used for irritancy testing. At 24, 48, 72, and 96 hour intervals, reactions are recorded.

### Evaluation of Cream

Rheology

Since that these lotions are sold in tubes or other containers, rheology is crucial. The viscosity or rheology ought to stay unchanged. Viscosimeters designed for such liquids can be used to test the viscosity of these items because they are typically non-Newtonian in nature.

Sensitivity

The usage of different kinds of compounds along with the sporadic use of hormones, antiseptics, etc., might cause skin sensitization or photosensitization. This needs to be evaluated first. This test is often performed on skin using an open or occlusive patch test. After a while, the test sample and a common market product are applied in various locations, and the results are compared. testing with biological agents

Phase Separation

By storing a specific amount in a graduated cylinder and measuring the volume of separated phase after predetermined time intervals, one may easily ascertain the pace and degree of phase separation in an emulsion. Globule coalescence or creaming may cause the phase separation. Centrifugation can



be used to speed up the phase separation test at low to moderate speeds. At most, one can anticipate a mixture of creamed and solidified particles, and accurate interpretations could be challenging in such a scenario.

### Effect of Thermal Stresses

It is usual to evaluate the stability of an emulsion by subjecting it to high and low temperatures in alternating cycles. The samples are first exposed to 60 C for a few hours and then to 0 to 40 C. Such exposures are repeated a number of times and emulsion stability assessed after each cycle. It is usual to evaluate the stability of an emulsion by subjecting it to high and low temperatures in alternating cycles. The samples are first exposed to 60 C for a few hours and then to 0 to 40 C. Such exposures are repeated a number of times and emulsion stability assessed after each cycle. An emulsion's stability is often assessed by submitting it to alternating cycles of high and low temperatures. After a few hours at 60 C, the samples are then exposed to 40 C. These exposures are conducted repeatedly, with each cycle ending with an evaluation of the emulsion's stability.

### Evaluation of Paste

#### Abrasiveness

Pastes or powders were mechanically brushed onto the teeth, and the results were examined through mechanical observation or other methods. Particle size often determined the abrasive nature.

#### Particle Size

This can be determined by microscopic study of the particles or other means.

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#### Cleansing property

This is investigated by evaluating how brushing with a dental cleaner (paste or powder) alters the reflectance nature of a lacquer coating on a polyester film. Additionally, an in vivo test has been proposed in which teeth were brushed for two weeks and the state of the teeth was evaluated using photos both before and after use.

#### Consistency

For the paste to be able to press out of the container, it is crucial that the paste maintain its consistency. Viscosity research is crucial for these powders straight out of the container.

#### PH of the product

A pH meter is used to measure the pH of the 10% product dispersion in water

#### Character Foaming

For dental pastes or tooth powders that create foam, this test is particularly necessary. A particular quantity of product can be combined with a predetermined amount of water and shaken. Studies are conducted on the nature, stability, and washability of the resulting foam.

### Evaluation on powder

#### Shade Control and Lighting

This is to monitor and assess the color shade variation across batches, and with the standard, appropriate testing must be carried out to avoid in colors. Comparing the appearance of the powder's body when it is spread out and flattened on a white paper background to a standard is one way to do this. Comparing the sample's skin tone or undertone to the standard is the other evaluation technique. The same puff that is used for the finished pack should be used to apply powders.

#### Dispersion of colour

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#### Pressure Testing

The compact powder should be subjected to uniform pressure so that a penetrometer can measure its hardness. The compact tablet's hardness is measured at multiple spots to ensure that the hardness is consistent.

#### Breakage Test

This is accomplished by repeatedly dropping the little powder tablet from a height of 8 to 10 inches onto a hardwood surface, then observing the breakage or clipping of the resistance against regular handling and travel.

#### Flow Property

This is crucial, especially for body powders, which should be easy to apply and simply come out of the container. This can be investigated by measuring the height and radius of the heap that forms, as well as the angle of repose of the powder product when it is allowed to descend from a funnel onto a plate.

### Evaluation on Suspension

#### Sedimentation of volume

Determining the volume of sedimentation and how easy it is to redisperse from the most popular fundamental evaluation techniques. Sedimentation volume is a straightforward idea. To put it briefly, it takes into account the ratio of the sediment's ultimate height (Hu) to the suspension's starting height (Ho) as the suspension settles in a cylinder under typical circumstances. The better the suspendability, the higher this proportion. To plot the Hu/Ho ratios as ordinates with time as the abscissa, first determine the ratios. Keep in mind that even though the height at any one time. The plot that was just described will begin at time zero, or 1.0, and the curve will either be horizontal or gradually slope downhill to the right over time. By comparing several formulas, one can determine which is best by looking at the lines; the better formulations will definitely produce lines.





## Evaluation of Lotion

### Antiseptic property

Since these preparations contain antiseptics, an in-vitro test is required to assess their antiseptic properties.

### Determination of alcohol content

Since these preparations contain alcohol, it is important to estimate the alcohol concentration, which can be done using any appropriate method.

## Evaluation of Gel

### Drug Content

A 50 ml volumetric flask containing 1 g of gel was precisely weighed, and 20 ml of filtered water was added while the flask was continuously shaken. Water and a mixture of 10% methanol were used to modify the volume. Similar procedures were also applied to plain bases in order to determine blanks. Using a UV spectrophotometer, the absorbance of the solution containing the blank was measured at 360 nm.

### Homogeneity of drug content

Six tubes were chosen at random and their contents were assayed as previously mentioned in order to ensure uniformity of the drug content. Research were conducted in triplicate, and data analysis was done using mean values.

### Spreadability

To assess spreadability, a modified apparatus with two glass slides with gel between them the upper one hooked to a balance and the lower one fastened to a wooden plate was utilized.

### Extrudability

A straightforward technique was used to calculate the weight in grams needed to extrude a 0.5 cm gel ribbon from the collapsible tube in 10 seconds, indicating extrudability.

## Evaluation of Suppository

### Melting range test

This test, also known as the macro melting range test, determines how long it takes for the complete suppository to melt in a water bath kept at a constant temperature of 37 degrees Celsius.

### Liquefaction or softening time test

It's made up of a U-tube that's partially immersed in a water bath that stays at a steady temperature. The suppository is held in place in the tube by a constriction on one side.

The "softening time" is measured by placing a glass rod on top of the suppository and timing how long it takes the rod to pass through to the constriction.

### Dissolution Test

It has always been challenging to test for the rate of drug material release from suppositories in vitro because of dispersion, melting, and distortion in the dissolution medium. In the beginning, testing was done as simple as placing in a beaker with a medium inside. Many strategies, such as separating the sample chamber from the reservoir with a

membrane or a wire mesh basket, have been used in an attempt to control the variance in the mass/medium interface. Studies have also been conducted on samples that are enclosed in dialysis tubes or natural membranes. The material has been held in place by flow cell apparatus using wire screening, cotton, and, most recently, glass beads.

Topical drug delivery refers to the process of treating local infections by applying a medication topically to the skin or mucous membrane.

Because of its noninvasiveness, excellent patient compliance, and lack of systemic toxicity, stomach

## CONCLUSION

1. Topical distribution is a favored administration method over alternative delivery systems because it reduces irritation or exposure of secondary tissues to the relevant substance.

2. Topical delivery faces several obstacles, such as the tight connection found in the stratum corneum and the rapid turnover of tissue fluids in areas like the nose, eyes, and vagina.

3. These barriers cause a medicine or foreign moiety to have less access to its target site, have shorter residence times, or cause a formulation to wash out of the application site more quickly.

4. To enhance the effectiveness of treatment, some novel formulations, like hydrogels, In published patents, bioadhesive patches, rings, lenses, masks, lipid-based carriers, and microneedles have all been shown. These technologies are still being investigated.

5. Developing innovative technologies and modifying formulation excipients can result in the creation of topical drug delivery systems that are safe, effective, and feasible for industry use.

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