

Topical ointment: an updated review

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ABSTRACT

The main advantage of topical delivery system is to bypass the first pass metabolism, avoidance of the risk and annoyance of intravenous therapy and of the varied conditions of absorption, like pH changes, gastric emptying time and presence of enzyme. The skin is an organ, which consists of the epidermis, the dermis and the hypodermis. Its main functions are to protect and enclose the body, to regulate body temperature, eliminate waste materials, aid in absorption and in the perception of stimuli such as touch, pain, temperature and pressure. The skin has a slightly acidic pH that ranges between 4 and 6. This forms an effective antiseptic layer and retards the growth of bacteria and fungi on the skin surface.

Key Words: Topical ointment, Skin, medicated ointment.

INTRODUCTION

Topical drug administration is a localized drug delivery system anywhere in the body through vaginal, ophthalmic, rectal and skin as topical routes. A dermatological delivery system is one that is applied to skin by inunction spraying or dusting. The topical or dermatological preparation are applied to the skin for their physical effects i.e. for their ability to act as skin protectants, cosmetics, lubricant, rubifaciant, counterirritant, astringent, cleansing agent, keratolytics and depilatory agents, altering pigmentation, sclerosing agents etc².

A large number of agents have been incorporated into the topical drug delivery system for their therapeutic effectiveness for local or systemic use that includes anesthetic, anti-inflammatory, corticosteroids, antibacterials, antifungal, scabicides, enemas, antileprotics and sunscreen agents.

Topical antibiotic agents are available in a variety of dosage forms mainly as creams, ointments, powders and dressings⁷. The dressings are generally impregnated with the antimicrobial agent and can be in the form of hydrogels, alginates or foam. Below is a list of some of the topical antibiotic options available on the South African market. These are available either as single agents or in combination.

ointment formulation provides better application property and stability in comparison to cream and gel. Topical ointment are deliberate for skin application or to certain mucosal surfaces for local action or percutaneous penetration of medicament or for their emollient or

defensive action. ointment are evaluated by subsequent parameters such as pH, viscosity, grittiness drug content, Spreadability, extrudability, homogeneity, skin irritation studies, in-vitro release, in Stability¹⁸.

Skin:

The skin has three layers. Beneath the surface of the skin are nerves, nerve ending, glands, hair follicles and blood vessels. A typical human skin surface is known to include, on the normal 40-70 hair follicles and 200-300 sweat ducts on every square centimeter of the skin.

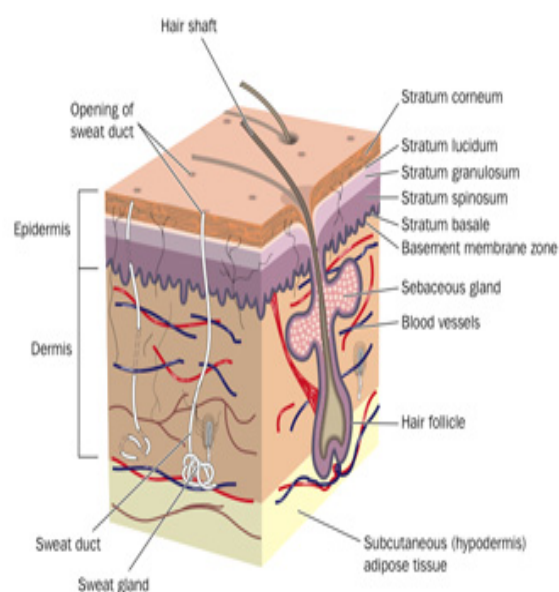


Figure 1: Structure of skin

Epidermis:

The epidermis is the relatively thin, tough, outer layer of the skin. Most of the cell in the epidermis are keratinocytes. The outermost portion of the epidermis, known as stratum corneum, is relatively waterproof and when undamaged, prevents most bacteria, viruses and other foreign substances from entering the body².

Dermis:

The dermis skin next layer is a thick layer of fibrous and elastic tissue mostly of collagen, elastin, and fibrillin give its flexibility and strength. the dermis contains nerve ending, sweat gland, oil gland, hair follicles and blood vessels².

Fat layer:

Below the dermis lies a layer of fat that helps insulate the body from heat and cold, provide protective padding and serve as an energy storage area².

Topical ointment:

Pharmaceutical ointments are semisolid systems that are applied externally, primarily to the skin and also to mucous membranes. Ointments are semisolid preparation intended for application to the skin with or without inunction. they may be oleaginous e.g., white ointment; they may be entirely free of oleaginous substances e.g., polyethylene glycol ointment, or they may be emulsions of fatty or wax like material containing relatively high proportion of water e.g., hydrophilic ointment.”

Ideal properties of topical ointment:

- Should be inert, compatible
- should not retard wound healing
- release the medicament efficiently at the site of application
- non-dehydrating, non-greasy and neutral in reaction
- compatible with common medicaments
- have minimum number of ingredients
- easy to compound and remain stable on storage
- economic and easy to transport

Classification of Topical medications:

1. Topical solution
2. Lotion
3. Shake lotion
4. Cream
5. Ointment
6. Gel

Factors affecting topical absorption of drugs:

1. Lipid water solubility
2. Concentration
3. Duration of contact
4. Solubility of medication

5. Physical condition of the skin

6. Part of the body exposed including the amount of hair on the skin

7. Nature of the skin

8. Nature of the pharmaceutical product

9. Drug mixing and drug storage

SELECTION OF THE BASE:

Selection of the base to use in the formulation of an ointment depends on careful assessment of a number of factors, including the following:

1. Desired release rate of the drug substance from the ointment base
2. Desirability of topical or percutaneous drug absorption
3. Desirability of occlusion of moisture from the skin
4. Stability of the drug in the ointment base
5. Effect, if any, of the drug on the consistency or other features of the ointment base
6. Desire for a base easily removed by washing with water
7. Characteristics of the surface to which it is applied

BASES OF OINTMENT:

1. Oleaginous bases: these bases consist of water insoluble, hydrocarbons vegetable oil, animal fats and waxes. The constituents of hydrocarbons bases are soft paraffin, hard paraffin and liquid paraffin. To incorporate an insoluble drug into these bases, mix the powder with a mortar and pestle. Use a oleaginous base to wet the powder and then mix the wetted powder into the ointment base. drug to be mix into the ointment will be much less than the amount of ointment. In other words, a small amount of drug will be mix into a large amount of ointment. The process of geometric dilution will "diluted" the drug into the ointment. It begins by incorporating the drug into an amount of ointment of approximately the same size. Soluble drugs can be incorporated into oleaginous bases by fusion. The base is liquefied over low heat (not to exceed 70°C) and then the drug is added to the molten base. The mixing ingredients is then allowed to cool with occasional stirring⁵.

Type of oleaginous base:

- Hydrocarbons
- Vegetable oils and animal fats
- Hydrogenated and sulphated oils
- Alcohols, acid and esters
- Silicones

2. Absorption bases: An absorption base is an oleaginous base that contains a w/o emulsifying agent. When water is taken up into the base, it will form a w/o emulsion. Absorption bases typically can incorporate

about 50% of their volume in water. Incorporating insoluble drugs into these bases can be done mechanically or by fusion. The final destination (internal or external phase of the emulsion) of the drug must be reconsidered when selecting a fine agent. If the drug will reside in the internal phase (water phase), then the fine agent should be water soluble or miscible. Water, glycerin, alcohol, or propylene glycol would be suitable fine agents. If the drug will reside in the external phase, then mineral oil should be used. Water soluble ingredients can be added to the water phase of the w/o emulsion⁵.

Types of absorption base:

- Cholesterol
- Cottonseed oil
- White petrolatum

3. Emulsion bases: these type base are two type-o/w and w/o.

- **O/W Emulsion Bases:** Water soluble powders can be directly incorporated into the external phase using a pill tile and spatula. If the powder is insoluble, the fine agent should be water miscible so glycerin, propylene glycol, polyethylene glycol (PEG) 300 or 400, or alcohol would be acceptable. If the insoluble substance has a different salt form that is aqueous soluble, consideration should be given to using that salt form⁶.

- **W/O Emulsion Bases:** Oils and insoluble powders can be directly incorporated into the external phase using a pill tile and spatula. If a fine agent is to be used with the insoluble powders, it should be miscible with the oil phase; mineral oil would be a suitable agent. fine agents may be needed with larger quantities of insoluble powders. If the insoluble powder has a different salt form that is oil soluble, consideration should be given to using that salt form⁵.

Most vegetable and animal fats and oils contain a small proportion of free fatty acid, which combines with alkaline substances to form a soap.

4. Water-soluble bases: Water soluble drugs can be dissolved in a small quantity of water and incorporated using a pill tile and spatula. Insoluble powders will require a water miscible fine agent such as glycerin, propylene glycol, or polyethylene glycol 400. Oils can be added into these bases by first mixing the oil with glycerin or propylene glycol, and then incorporating the mixture into the base. Heat may be necessary if the quantity of liquid to add to the base is large³.

Types of water-soluble base:

- Glyceryl monostearate(GMS)
- Cellulose derivatives

- Sodium alginate
- Bentonite
- Carbopol 934

Physical method of topical drug delivery for ointments:

Intophoresis:

This method involving the transport of ionic, charged molecules into a tissue by the passage of direct or periodic electric current through an electrolyte solution containing the ionic molecules to be delivered use an appropriate electrode polarity.

Electroporation:

This method in process involves the application of transient high voltage electrical pulse to cause rapid dissociation of the stratum corneum through which large and undersized peptides, oligonucleotides and supplementary drugs can exceed in considerable amounts.

Sonophoresis:

Sonophoresis method in the use of the regularity ultrasound waves.

Phonophoresis:

This method in movement of drugs through living intact skin and into soft tissues under the ultrasound perturbation is called phonophoresis.

Vesicular concept:

This method in drug close in vesicle made from phospholipids and nonionic surfactants are used for transport of drug into and across the skin.

Microfabricated microneedles method:

This technology employed micron-sized needles made silicon. These microneedles after incorporation into the skin create conduits for transfer of drug through the stratum corneum.

PREPARATION OF THE OINTMENTS:

Two type of method for preparation of ointments. Mechanical method and Fusion method.

1. Mechanical method: The quantity of ointment is not more than 50 g, white porcelain or marble ointment should be used in conjunction with a flexible steel spatula. A steel spatula should not be used as medicament may react with the metal. the substance react with metal such as mercury compounds, tannic acid, salicylic acid and iodine⁴.

2. Fusion method: Ointment containing hard paraffin, beeswax, emulsified wax, wool alcohol are prepared by melting ingredients in a porcelain dish over a water bath. In this process higher melting point substance should be melted first and add then other ingredients of the bases in order of their melting point⁴.

Factors governing selection of the ointment base: two type factors governing selection of the ointment base. dermatological factors and pharmaceutical factors.

A. Dermatological factors: dermatological factors are sub divided.

1. Absorption and penetration.
2. Effect on skin function.
3. Miscibility with skin secretion and serum.
4. Compatibility with skin secretions.
5. Irritant effect.
6. Emollient properties.
7. Removal.

B. Pharmaceutical factors:

1. Stability.
2. Solvent properties.
3. Emulsifying properties.
4. Consistency.

Evaluation method of ointments:

- Organoleptic properties
- pH
- Drug content
- Spreadibility
- Consistency of an ointment
- Stability study
- Tube extrudability
- Viscosity
- *In-vitro* drug release

Viscosity:

Viscosity is another type of bulk property defined as a liquid's resistance to flow. When the intermolecular forces of attraction are strong within a liquid, there is a larger viscosity. Viscosity can be not only a fluid's resistance to flow but also a gas' resistance to flow, change shape or movement. The opposite of viscosity is fluidity which measures the ease of flow while liquids such as motor oil or honey which are "sluggish" and high in viscosity are known as *viscous*.

Measuring Viscosity:

There are numerous ways to measure viscosity. One of the most elementary ways is to allow a sphere, such as a metal ball, to drop through a fluid and time the fall of the metal ball: the slower the sphere falls, the lower the viscosity that is measured. Another more advanced design of measuring viscosity known as the Ostwald Viscometer that is much more accurate than dropping a metal ball. An Ostwald Viscometer consists of two reservoir bulbs and a capillary tube. The viscometer is filled with liquid until the liquid reaches the mark A with the aid of a pipette to accurately measure out the volume of needed liquid⁵.

***In-vitro* drug release:**

In vitro release of API from topical and transdermal products, and subsequent permeation through a membrane, can be tested in a vertical diffusion cell (i.e. Franz diffusion cell). In this apparatus, formulation is applied or put in contact with a membrane that is in contact with a receiving medium. The receiving medium is sampled as a function of time and API is quantitated to determine a permeation/flux profile. Membrane materials include synthetic polymer, cadaver or animal skin, and tissue constructs. The choice of membrane is driven by the purpose of the test (i.e. development vs. quality control) and robustness of the model. This technique is applicable not only to externally applied topical formulations, but also to products that deliver via the vaginal, rectal, buccal, or nasal routes.

CONCLUSION:

Topical product used for the treatment of common skin infection. Ointment play important role in the topical drug delivery system. they decrease the systemic side effect, prolong and pronounced local action, and also avoids the first pass metabolism. Various formulations of ointments are taken for optimization in relation to ointment base consistency, ointment stability, stability with antioxidant, stability with different preservatives, better diffusion, and antifungal and antiseptic properties.

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