

A Review Ontopical Cream

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I. INTRODUCTION

- Topical drug administration is a localized drug delivery system anywhere in the body through ophthalmic, rectal, vaginal and skin as topical routes. These are applying a wide spectrum of preparations for both cosmetic and dermatological, to their healthy or diseased skin. These formulations range in physicochemical nature from solid through semisolid to liquid.
- Drug substances are seldom administered alone, but rather as part of a formulation, in combination with one or more non medicated agents that serve varied and specialized pharmaceutical function. Drugs are administered topically for their action at the site of application or for systemic effects.
- Drug absorption through the skin is enhanced if the drug substance is in solution, if it has a favorable lipid/water partition coefficient and if it is a nonelectrolyte. For the most part, pharmaceutical preparations applied to the skin are intended to serve some local action and as such are formulated to provide prolonged local contact with minimal systemic drug absorption.
- Drug applied to the skin for their local action include antiseptics, antifungal agent, skin emollients and protectant. The main advantages of topical delivery system are to bypass first pass metabolism. Avoidance of the risks.
- Fungal infections of skin are one of the often-faced dermatological diseases in worldwide. Topical therapy is an advantageous treatment choice for the cutaneous infections due to targeting of drugs to the site of infection and reduction of the systemic side effects.^[3]
- A number of formulation strategies have been investigated for delivering antifungal compounds through targeted site of the skin. The purpose of topical dosage forms is to conveniently deliver drugs to a localized area

of the skin and microemulsions can be used to deliver drugs via several routes and their composition and structure enables them to incorporate greater amount of drug than other topical formulations.^[1]

- Topical agents that are conventionally used for the treatment of skin fungal infections are usually formulated as creams, lotions or gels. They either exhibit fungicidal or fungistatic actions depending on the agent being delivered. Since the side effects of fungal agents applied topically are less than their oral counterparts, they are the preferred agents.
- Another advantage of topical formulation is that it avoids drug-drug interactions, which are more common in case of oral administration.
- A drug must have some specific characteristics to be delivered in the form of a topical preparation for treatment of skin fungal infections; the most important of these is its lipophilic nature. When such a drug is applied on the skin, a depot is formed in the lipidic stratum corneum which releases the drug slowly to the underlying skin layers, that is, epidermis and dermis. Therefore, in order to achieve a topical effect for an antifungal drug, the release rate of this lipophilic drug should be controlled by the formulation in order to achieve high local therapeutic concentration and to provide prolonged pharmacological effect.
- Another important consideration is the molecular weight of the drug; this is especially important for antifungal drugs known to exceed 500 Da such as amphotericin B and ketoconazole. These considerations have led to the development of several carriers which were found to improve topical drug delivery by either finding a way into a shunt such as hair follicle, accumulating between corneocytes, and intermingling with skin lipids, or by disintegrating and merging with lipidic layers.

- intermingling with skin lipids, or by disintegrating and merging with lipidic layers. Whether their size was in the micrometer or nanometer range, carrier systems were found to impart desirable characteristics to topical formulations of antifungal drugs.^[2]
- Human infections, particularly those involving skin and mucosal surface constitute serious problems. The drug resistant bacterial and fungal pathogens have further complicated the treatment of skin infections. Topical route is most suitable route for skin infections^[3]
- Creams may be considered pharmaceutical products as even cosmetic creams are based on techniques developed by pharmacy and unmedicated creams are highly used in a variety of skin conditions (dermatoses). The use of the Fingertip unit concept may be helpful in guiding how much topical cream is required to cover different areas.^[12]
- Over the last decades the treatment of illness has been accomplished by administering drugs to human body via various routes namely oral, sublingual, rectal, parental, topical, inhalation etc. Topical delivery can be defined as the application of a drug containing formulation to the skin to directly treat cutaneous disorder or the cutaneous manifestations of a general disease (e.g.:- psoriasis) with the intent of containing the pharmacological or the effect of drug to the surface of the skin or within the skin semi- solid formulations in all their diversity dominate the system for topical delivery, but foams, spray, medicated powders, solutions and even medicated adhesive systems are in use.^{[13][14]}
- Creams have been used as topical preparations since time immemorial due to their ease of application to the skin and also their removal. Pharmaceutical creams have a variety of applications ranging from cosmetic purposes such as cleansing, beautifying, altering appearance, moisturizing etc. to skin protection against bacterial, fungal infections as well as healing cuts, burns, wounds on the skin.^[15]

ADVANTAGES

1. Avoidance of first pass metabolism.
2. Convenient and easy to apply.
3. Avoid of risk.
4. Inconveniences of intravenous therapy and of the varied conditions of absorption like Ph changes presence of enzymes gastric emptying time etc.

5. Achievement of efficacy with lower total daily dosage of drug by continuous drug input.
6. Avoid fluctuation of drug levels inter- and intra-patient variations.
7. They give prolong contact in their site of application than any other pharmaceutical semisolid dosage forms.
8. Injured area can be dried quickly by creams than other semi-solid preparations.
9. Easily water washable. Easy to wipe away.
10. Less greasy compared to ointment.

II. LIMITATIONS

1. Skin irritation of contact dermatitis may occur due to the drug and / excipients
2. Poor permeability of some drugs through the skin
3. Possibility of allergic reactions
4. Can be used only for drugs which require very small plasma concentration for action
5. Enzyme in epidermis may denature the drugs
6. Drugs of larger particle size not easy to absorb through the skin

TYPES OF CREAMS

Creams are those emulsions which are either,

1. oil in-water
2. water in-oil type

[Depending upon the main ingredients and purpose of these formulation]

Types of skin creams

1. Make-up Creams (o/w emulsions)

- Vanishing Creams
- Foundation Creams

2. Cleansing creams (w/o emulsions)

3. Creams for winter (w/o emulsions)

4. Cold creams for dry skin

- Moisturizing creams

5. All-purpose creams

6. Night creams

7. Skin protective and hand creams

Materials Used In Cream Preparation

Basic raw material in the manufacture of skin creams is, this includes

- Water
- petroleum oil
- vegetable oils,
- fats as well as their derivatives
- humectants and emulsifying agent.

1. WATER

- One of the most widely used raw materials in the manufacture of cream is water. In cosmetics water is used as solvent for many ingredients of cosmetics.
- Water should be either deionized or distilled, if it has to be incorporated in cream formulations.
- Water is cheapest ingredient in creams, so it is good judgement to use purest water.

2. OIL, FATS, WAXES

- Oil, fats and waxes and derivatives their form comprise an essential portion of creams
- Oil may be two types' mineral and glyceride.

Mineral oil

Mineral oil consists of hydrocarbons derived from petroleum oil. A number of mineral oils are used in cream formulation.

Examples:

- o Light liquid paraffin
- o Heavy liquid paraffin

Glyceride oil

Glyceride oil is mostly vegetable oils. Examples of glyceride oils are almond oil, arachis oil, _castor oil, coconut oil, olive oil etc.

Fats

A variety of fatty materials are used in cream preparations. These materials may be from vegetable, animal or mineral origin. Glyceride oils and fats may be of animals or vegetable origin. They consist of combinations of higher fatty acids and glycerin. When saponified they form soap, or fatty acid and glycerin, depending upon process used. The most common of these fatty acids are lauric, margaric, palmitic, stearic, saturated group. Oleic acid is liquid and most popular unsaturated fatty acid. More specially the oil most commonly used in other cosmetics are olive oil, almond oil, sesame oil, peanut oil, cocoa butter fat, mutton tallow, lard and beef stearin.

Waxes

Waxes used in creams and other cosmetics include beeswax, carnauba wax, ceresin, ozokerite japan wax and spermaceti. Of these beeswax and spermaceti are of animal origin, while carnauba, candelilla and japan wax are from vegetable kingdom. Montana a vegetable wax and ozokerite a mineral wax, are both derived from lignite of these

waxes. Beeswax, ceresin and spermaceti most important for cosmetics.

3. LANOLIN

Lanolin is derived from wool fat. The anhydrous grade is free from water. The hydrous lanoline contains between 25% and 30% water. Anhydrous lanolin has melting point of 380C to 420C and a slight odor.

4. GLYCOL

Those used in cosmetics consist mainly of ethylene glycol, diethylene glycol and propylene glycol. Glycol are dihydric alcohols lying halfway between ethanol and glycerol. There are number of glycol available.

5. COLOUR

Coloring agents is in fact, a generic term for any color imparting substances. Most of natural colors have been replaced by coal tar colors so far as cosmetics is concerned. A few of the natural colors might still to be used. Examples of natural Colors used in cosmetics are saffron, chlorophyll, cochineal.

6. EMOLLIENTS

Emollients, also commonly referred to as moisturizers, are products that help to soften skin or to treat skin that has become dry. Most emollients are forms of oil or grease, such as mineral oil, squalene, and lanolin. They work by increasing the ability of the skin to hold water, providing the skin with a layer of oil to prevent water loss, and lubricating the skin.

7. EMULSIFYING AGENT

Inorganic solid

Inorganic solid which forms emulsion include bentonite, colloidal, kaolin, hydrated lime or magnesia and other clay, when dispersed with water, their colloidal properties permit the formation of emulsion in water.

Gums and proteins

Gums and proteins are used as emulsifying agent include gum tragacanth, karaya gum, gum Arabic, agar- agar, Irish moss, alginate pectin, saponins, gelatin, casino, methyl cellulose and egg albumin.

8. WETTING AGENT

Wetting agent are basically a type of surface-active agents. Among them are include soap, sulfonated oils, fatty alcohols sulfates, sulfated fatty esters and amides, Secondary alcohol sulfates and aryl alkyl sulfates. Quaternary ammonium compound are series of wetting agents which also exhibit high germicidal and fungicidal properties. Wetting agent have two common properties of lowering surface tension, being uninfluenced by hard water forming considerable foam with water and other solvents, possessing considerable solvent action and aiding in formation of emulsions.

9. HUMECTANTS

Humectants (or moisturizers) are important cosmetic ingredients allowing to prevent loss of moisture thereby retaining the skin's natural moisture. Some compounds also have the ability to actively attract moisture. Humectants are key ingredients in most skin care products but are also often used in hair care products to volumize the hair by attracting moisture which expands the hair shaft. There is a large variety of very different compounds providing moisturizing effects including proteins, acids, polysaccharides, and various small molecules (e.g., glycerin, sorbitol, urea, aloe Vera, olive oil, honey, babassu oil, grape seed oil, avocado oil, etc.).

10. PERFUMES

Perfume is a substance that imparts a scent or odor, including a sweet and pleasant smell.

Examples of natural perfumes used in creams are

- White Blossoms
- Rosy Dreams
- Orange Blossom

PREPARATION [General procedure of manufacturing]

As these preparations are emulsion type, the total ingredients can be classified in to oil phase and aqueous phase. Ingredients of oil phase and aqueous phase. Ingredients of oil phase should be taken in increasing melting point. The materials of least melting point should be taken in increasing melting point. The materials of least melting point should be taken and melt it. Add the other oil or wax gradually in increasing melting point and melt them with continuous stirring. Take separately the ingredients of aqueous phase and mix them and heat to same temperature as oil phase. Emulsifying agent be added to specific phase. Mix the two phases with continuous stirring until a smooth

cream is formed Finally the Product can be milled by triple roller mill. Preservative should be dissolved in the water before making cream. Perfume should be added after the primary cream is formed and cooled but before final milling^[6]

III. EVALUATION

Physical Evaluation of the Cream

1. Organoleptic Characteristics. All blank formulations (i.e., formulations without any active ingredients or preservatives) and drug-loaded formulations were tested for physical appearance, colour, texture, phase separation, and homogeneity. These characteristics were evaluated by visual observation. Homogeneity and texture were tested by pressing a small quantity of the formulated cream and gels between the thumb and index finger. The consistency of the formulations and presence of coarse particles were used to evaluate the texture and homogeneity of the formulations. Immediate skin feel (including stiffness, grittiness, and greasiness) was also evaluated.

2. Determination of pH: The pH of the cream can be measured on a standard digital pH meter at room temperature by taking adequate amount of the formulation diluted with a suitable solvent in a suitable beaker.

3. Physical appearance: The physical appearance of the cream can be observed by its color, roughness and graded.

3. Spread ability: Adequate amount of sample is taken between two glass slides and a weight of 100gm is applied on the slides for 5 minutes. Spread ability can be expressed as, $S = m \cdot l / t$

Where,

m = weight applied to upper slide.

l = length moved on the glass slide.

t = time taken.

4. Saponification value: 2gm of substance refluxed with 25ml of 0.5 N alcoholic KOH for 30min, to this 1ml of phenolphthalein added and titrated immediately, with 0.5N HCl, note the reading as 'a'. Repeat the operation omitting the substance being examined. Note the reading as 'b'. Saponification value = $(b-a) \cdot 28.05 / w$ Where, w = weight of substance in gram.

5. Acid value: 10gm of substance is dissolved in accurately weighed 50ml mixture of equal volume of alcohol and solvent ether, the flask was connected to reflux condenser and slowly heated, until sample was dissolved completely, to this 1ml

of phenolphthalein added and titrated with 0.1N NaOH, until faintly pink color appears after shaking for 30 seconds. Acid value = $n \times 5.61/w$ Where, n = the no. of ml of 0.1 N KOH solution. w = the weight of substance in gram.

6. Viscosity: Viscosity of formulated creams can be determined by using Brookfield Viscometer.

7. Homogeneity: The formulation was tested for the homogeneity by visual appearance and by touch.

8. Removal: The ease of removal of the creams applied was examined by washing the applied part with tap water.

9. Dye test: The scarlet dye is mixed with the cream. Place a drop of cream in a slide and cover with a cover slip and examine it under a microscope. If the disperse globule appears red and the ground colorless then it is o/w type and the reverse condition appears in w/o type of creams.

10. After feel: Emollience, slipperiness and amount of residue left after the application of fixed amount of cream was checked.

11. Type of smear: After application of cream, the type of film or smear formed on the skin were checked.

12. Irritancy study: Mark an area of 1sq.cm on the left-hand dorsal surface. The cream was applied to the specified area and time was noted. Irritancy, erythema, edema was checked, if any, for regular intervals up to 24hrs and reported.

13. Accelerated stability study: Accelerated stability study is conducted for formulation according to ICH guidelines.

14. In Vitro Release Test (IVRT)

• IVRT is well established for characterizing and evaluating the performance of semi-solid dosage forms. • IVRT can be a sensitive and discriminating method that is generally responsive to physicochemical changes in semisolid drug products.

• IVRT serves as a valuable tool for the demonstration of comparative in vitro drug release rates between the test and reference products.

• IVRT is not expected to correlate with or be predictive of in vivo bioavailability or bioequivalence.

Conducting an IVRT

The IVRT pivotal study comparing the [drug] release rates between the test and RLD products should be performed in a manner compatible with the general procedures and statistical analysis method specified in the United

States Pharmacopeia (USP) General Chapter, Semisolid Drug Products – Performance Tests.

IV. CONCLUSION

The skin is the most accessible part of the body and as such is also highly vulnerable to injuries. In case of cuts, burns and wounds, topical formulations such as creams are the most preferred for treatment. As compared to other conventional systems, topical formulations have certain advantages including- ease of application, less chances of side effects, non-invasive process and higher patient compliance. Research and development for the formulation of pharmaceutical creams for wound healing purpose has grown in recent decades owing to its obvious benefits. With the progress in the pharmaceutical field and industry, it is assured that pharmaceutical creams will still be an interesting and appealing area of research for years to come.

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