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TOICAL DRUG DELIVERY SYSTEM: FORMULATION AND EVALUATION OF CREAM

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ABSTRACT

Creams are considered an important part of cosmetic product as topical preparations from time immemorial due to their ease of application to the skin and also their removal. From cosmetic purposes, Pharmaceutical creams have a variety of applications 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. These semi solid preparations are safe to use by the public and society. cream with suitable methods of preparation of creams, their classification based on their function, their advantages and disadvantages, characteristics and the various types of creams, ingredients used in the formulation of creams and their various evaluation parameters.

KEYWORDS: Skin, Topical drug delivery, Cream, Types of cream, Evaluation.

1. INTRODUCTION

The appearance and function of the skin are maintained by an important balance between the water content of the stratum corneum and skin surface lipids.[1-2] The skin represents the most superficial layer of the body, and so it is constantly exposed to different environmental stimuli.[3] Exposure to external factors as well as endogenous factors may disrupt this balance.[4-6] In addition, frequent use of soaps, detergents and topical irritants such as alcohol and hot water can remove the skin surface lipids.[7] Disruption of skin barrier led to the various type of skin problems most common condition is a loss of water content which leads to dryness of skin such as roughness, scaling, cracks, redness and an uncomfortable feeling of tightness, sometimes with itching and stinging.[8] Treatment with moisturizer aims at

maintaining skin integrity and well-being by providing a healthy appearance of the individual. Numbers of moisturizers are available under the label of natural, safe, organic, herbal while the basic properties of humectancy, occlusivity and emolliency are consistent across all moisturizers.[9] Most of the available moisturizers use synthetic adhesives, emulsifiers, perfuming agents, pigments, surfactants and thickeners to form the base. There is extensive need to replace toxic synthetic agent from the base using natural agents.[10-11]

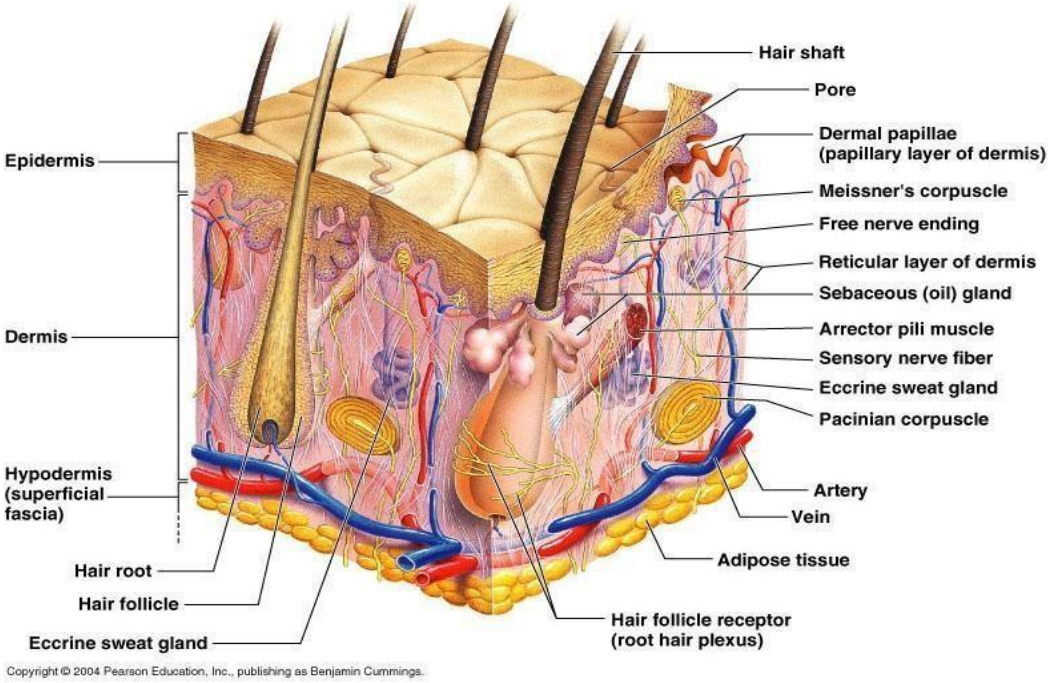

Fig. 1: Anatomy of skin.

2. Topical drug delivery

Over the last decades the treatment of illness have been accomplished by administrating drugs to human body via various roots 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 (eg:-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.

(kavitha et al, 2003)[21]

Advantages of topical drug delivery systems[1, 4]

- Avoidance of the first pass metabolism.
- Convenient and easy to apply.
- Avoidance of risks and inconveniences of the intravenous therapy and of diverse conditions of absorption like pH changes, presence of enzymes, gastric emptying time.
- Easily terminate the medications, when needed.
- Deliver drug more selectively to a specific site.
- Avoidance of the gastro-intestinal incompatibility.
- Providing utilization of drugs with short biological half life, narrow therapeutic window.
- Improved patient compliance.
- Provide suitability for self-medication.
- Achievement of effectiveness with lower total daily dose of drug by continuous drug input.
- Prevents fluctuation in drug levels, inter- and intra patient variations.
- A quite large area of application in comparison with buccal cavity.
- Ability to deliver drugs more selectively to a specific site.[1,4]

Disadvantages of topical drug delivery systems

- Skin irritation or dermatitis may occur due to the drug or excipients.
- Poor permeability of some drugs through skin.
- Drugs with larger particle size can't be easily absorbed through the skin.
- Possibility of allergic reactions.[5]
- Can be used only for those drugs which need very small plasma concentration for action The route is not suitable for those drugs that irritate or sensitize the skin.[1,4,5]

3. Creams

Creams are the topical preparations which can be applied on the skin. Creams are defined as "viscous liquid or semi-solid emulsions of either the oil-in-water or water-in-oil type" dosage forms which consistency varies by oil and water.[6] Creams are used for cosmetic purposes such as cleansing, beautifying, improving appearances, protective or for therapeutic function. These topical formulations are used for the localized effect for the delivery of the drug into the underlying layer of the skin or the mucous membrane. These products are designed to be used topically for the better site specific delivery of the drug into the skin for skin disorders.[7]

Creams are considered as a pharmaceutical product as they are prepared based on techniques developed in the pharmaceutical industry; unmedicated and medicated creams are highly used for the treatment of various skin conditions or dermatoses. Creams can be ayurvedic, herbal or allopathic which are used by people according to their needs for their skin conditions. They contain one or more drugs substances dissolved or dispersed in a suitable base. Creams may be classified as o/w or w/o type of emulsion on the basis of phases. The term 'cream' has been traditionally applied to semisolid formulated as either water-in-oil (e.g.: cold cream) or oil-inwater (e.g.: vanishing cream).[8]

4. Types of skin creams

They are divided into two types

Oil-in-Water (O/W) creams: Which are composed of small droplets of oil dispersed in a continuous phase, and an emulsion in which the oil is dispersed as droplets throughout the aqueous phase is termed an oil-in-water (O/W) emulsion.

Water-in-Oil (W/O) creams: Which are composed of small droplets of water dispersed in a continuous oily phase. When water is the dispersed phase and an oil the dispersion medium, the emulsion is of the water-in-oil (W/O) type.[9-11]

5. Classification of creams

All the skin creams can be classified on different basis

1. According to function, e.g. cleansing, foundation, massage, etc.
2. According to characteristics properties, e.g. cold creams, vanishing creams, etc.
3. According to the nature or type of emulsion.

Types of creams according to function, characteristic properties and type of emulsion

1. Make-up cream (o/w emulsion): a) Vanishing creams. b) Foundation creams.
2. Cleansing cream, Cleansing milk, Cleansing lotion (w/o emulsion)
3. Winter cream (w/o emulsion): a) Cold cream or moisturizing creams.
4. All-purpose cream and general creams.
5. Night cream and massage creams.
6. Skin protective cream.
7. Hand and body creams.

1. Make-up cream

These are mainly o/w type of emulsion. It is cream-based product which leaves a smooth hydrated finish (either stain matte or luminous) on the skin. It nourishes skin andis basically sweat-resistant and creates a dewy sheen.

- **Vanishing creams:** They are called vanishing creams because they seem to disappear when rubbed onto the skin. These formulations are based on stearic acid. After application, the cream leaves a dry but tacky residual film which also has a drying effect on the skin. Because of this reason, these are used particularly in hot climates which cause perspiration on the skin.

- **Foundation creams:** These cream serve as a foundation base for make-up. It acts as an adherent base for application of make-up powders. They provide emollient action and a protective action against environment to the skin which is neither too greasy nor too dry. It is multicoloured make up applied on the face to create an even, uniform colour similar to the complexion, to cover flaws and to change the skin tones.

2. Cleansing creams

These creams are used for body cleaning purposes and it is used for personal hygiene and beautification which is important for cosmetics. Cleansing creams or lotions can be used for the removal of make-up, surface grim, oil mainly from the face and neck.

3. Winter creams

These are w/o type of formulation and in this formulation oil content will be more than water content. These creams are mainly used for chapped and dry skin. Cold cream: It is known as moisturizer or moisturizing cream. Cold cream must have an emollient action. It should produce a cooling sensation in use and the oil film on the skin should be nonocclusive.

4. All purpose Creams and General creams

These creams are used more nowadays than before. These creams are somewhat oily but nongreasy type and can spread on the skin easily. This can also be used as a night creams, nourishing creams, protective creams for prevention or alleviation of sunburns or for the treatment of roughened skin areas.

5. Night cream or massage creams

These creams are mainly used for the nourishing the skin or as a treatment to dry skin. Creams which are generally applied on skin and left for few or several hours over night are mainly known as night creams. Creams which acts as an emollient by rubbing the cream on the skin with massage is known as massage cream.

6. Skin protective creams

These creams are smooth, thick bodied creams formulated to provide an invisible, uniform protective film barrier to the skin. It helps to maintain the barrier between the skin and contaminants that may irritate the skin (contact dermatitis and occupational dermatitis). Strengthens the natural properties of the skin and maintains the balance of normal to combination skin.

7. Hand and Body creams

Hands are one of the first places to show signs of aging. We tend to wash our hand several times a day, stripping off moisture. Applying cream softens and protects the skin and it keeps the skin looks younger. Since the skin on our palms and fingers needs oil to stay supple and to prevent it from chapping and cracking, it is sensible to use hand creams that puts plenty of oil back in. It is used on the hands more than other parts of the body.[12-15]

6. Methods of preparation of creams

- **Preparation of o/w emulsion cream:-** The oil soluble components and the emulsifier are taken in one beaker and melted in a water bath at 75°C. And in other beaker water, preservatives and watersoluble components are taken and melted at 75°C. After heating, the oil phase was taken in a mortar and pestle and slowly the water phase was added and triturated till clicking sound was heard. Finally, when the temperature cools down, perfuming agents and/or preservatives are added. In this preparation, water content will be more than the oil.
- **Preparation of w/o emulsion creams:-** The oil soluble components and the emulsifier are taken in one beaker and melted at 75°C. And in another beaker water and water soluble components are taken and melted at 75°C. After melting, water phase are taken in mortar and pestle and slowly oil phase was added and triturated till clicking sound was heard. And when the temperature of the cream will get cooled, then the perfuming agent are added. In this preparation, water phase will be less and oil phase will be more.[64]

7. **Formulation table**

Table 1: Formulation table.

Sr. No.	Name of ingredients	Quantity for 100 gm
1.	Beeswax	8.0 gm
2.	Mineral oil	49.0gm
3.	Paraffin wax	7.0 gm
4.	Cetyl alcohol Borax	1.0 gm
5.	Water	0.4 gm
6.	Preservative	34.6 gm
7.	Perfume	q.s.
8.		q.s.

2. **Evaluation parameters of creams**

1. **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.
2. **Physical appearance:** The physical appearance of the cream can be observed by its colour, roughness and graded.
3. **Spreadability:** Adequate amount of sample is taken between two glass slides and a weight of 100gm is applied on the slides for 5 minutes. Spreadability can be expressed as, S= m*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)*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 colour appears after shaking for 30 seconds. Acid value = n*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 colourless then it is o/w type and the reverse condition appears in w/o type of creams.
10. **Skin hydration test:** Hydration of the epidermis was determined with a non-invasive using an electronic device, Multitester [CASIO, H-21, India] that measured resistance based on the commonly known fact that hydrated skin has less resistance to current flow than dehydrated skin. The level of stratum corneum hydration was assessed by measurement of the changes in skin resistance and is referred to as the galvanic skin response or electrical skin resistance. The skin resistance reported in ohms with electrodes [size 1 cm^2] was measured 30min and 6hr after application of the formulation [continuously upto 3weeks] at 1000 khz, 10mA, AC.[34]

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