



Review on cream as topical drug delivery system

Siddhant Hagavane*, Sneha Sonawane, Akshay Katkale, Vishvam Kunde
SMBT College of Pharmacy, Nandi-Hills, Dhamangaon, Nashik, Maharashtra, India

Abstract

Creams are considered an important part of cosmetic product as topical preparations from cosmetic purposes, pharmaceutical creams having a various variety of applications for ex. Beautifying, moisturizing, cleansing etc. for skin protection against bacterial and fungal infections. Creams are for the most part solid or liquid emulsions. If they set solid, they are emulsified in molten state by heating the ingredients to liquify them and permitting them to solidify after being filled into the packages. As already indicated, these emulsions either oil in water or water in oil types. The former type of emulsion predominates in the cream field. The introduction of numerous new emulsification aids and cream bases has made possible in recent years a greater variety of creams than was formerly possible. By numerous combinations of these newer products with the old bees' wax-mineral oil-borax-water cream type innumerable cream formulae may be devised. Creams have the number of advantages like easy to apply, more effective compares to other avoid risk. The functions of skin creams are to protect the skin against harshness from the environment and any dry conditions of the skin.

Keywords: creams, semisolid, formulation, cosmetic, topical, skin care, moisturizer

Introduction

The word 'Cosmetic' derived from a Greek word – 'kosmesticos' that means to adorn. From that time any actually stems from its use in Ancient Rome. Cosmetics products have been generally defined as "articles intended to be applied to the human body by being rubbed, poured, sprinkled, or sprayed for cleansing, promoting attractiveness, beautifying, or altering the appearance". Cosmeceuticals are cosmetic products having some specific therapeutic effects. They were typically produced by female slaves known as "cosmetae" which is where the word "cosmetics" stemmed from. Cosmetics are used to enhance appearance. Makeup has been around for many centuries. The first known people who used cosmetics to enhance their materials used to beautification or promoting appearance is known as cosmetic [1].

The word "cosmetics" beauty were the Egyptians. Makeup those days was just simple eye coloring or some material for the body. Now-a-days makeup plays an important role for both men and women. The importance of cosmetics has increased as many people want to stay young and attractive. Cosmetics are readily available today in the form of creams, lipstick, perfumes, eye shadows, nail polishes, hair sprays etc. Other cosmetics like face powder give glow to the skin after applying the base cream. Then we have lipsticks, which are applied by many women of all ages [2, 3]. They are made from wax and cocoa butter in the desired amount. Cosmetics like creams, gels, and colognes are used on a daily basis by both women and men. Creams act as a cleanser for the face in many circumstances. More recently anti-ageing creams have been manufactured which can retain younger looking skin for many years. The best cleansing agents are cleansing cream, soap and water. Cosmetic creams serve as a skin food for hard, dry and chapped skin. It mainly lubricates, softens and removes unwanted dirt from the skin. Some popular fat creams that are used include Vaseline and Lanolin. Dry creams are used in the manufacture of soap and gelatin which is used as a base for the skin. Hair care has become one of the fastest developing markets in the beauty industry. Many young men turn to oils and gels to maintain and style their hair. Products like hair gels, oils, and lotions have been introduced in the market to help protect hair fall and dandruff. Some professions, like the show business industry, focus on the importance of the outer appearance. Many personalities and artists have utilized makeup to beat the harsh lights and the glare of camera flashes. They very well know the importance of their looks and maintain them by using a variety of cosmetics. Recent research has shown that makeup helps in protection from harmful rays of the sun. Many beauty products manufacturers have utilized the needs of people to protect themselves and their skin from the rays of the sun. Many beauty products manufacturers have utilized the needs of people to protect themselves and their skin from the rays of the sun. The Importance of Cosmetics Today Cosmetics help to enhance our appearance and make us feel more confident. With more cosmetics on the market today than ever before, it becomes obvious to us that they play a great role in our everyday life [2].

Over the last decade, the treatment of illness has been accomplished by administrating drugs to the human body via different roots like oral, rectal, parental, inhalation, sublingual, topical, etc. The cream is the TDDS that can be applied to skin for the localized effect. It is a semisolid dosage form are prepared by techniques developed in the pharmaceutical industry. It is a mixture of two-phase e.g. (O & W) phase which are mixed to formulate final

preparation of cream by continuous stirring. These topical formulations are help to the deliver the active medicament in to the mucous membrane or the inner layer of the skin. the cream can be formulated as an ayurvedic, herbal, or allopathic which are used as per their need for their skin conditions. The cream may be classified as an o/w and w/o type of emulsion [3, 4].

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 [5]. 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 [6]. 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- in- water . (e.g vanishing cream) [7].

Anatomy of Skin

The skin is the largest organ of the body, accounting for regarding 15% of the overall weight. It performs several very important functions, together with protection against external physical, chemical, and biological assailants, similarly as prevention of excess water loss from the body and a role in thermoregulation. The skin is continuous, with the mucous membranes lining the body’s surface.[8] The system is made by the skin and its by-product structures. The skin composed of three layers: the epidermis, the dermis, and subcutaneous tissue. The outermost level, the epidermis, consists of a selected constellation of cells called keratinocytes, that perform tosynthesize albuminoid, along, threadlike supermolecule with a protecting role. The middle layer, the dermis, is fundamentally made up of the fibrillar structural protein known as collagen. The dermis lies on the connective tissue tissue, or panniculus, that contains tiny lobes of fat cells called lipocytes. The thickness of those layers varies significantly, betting on the geographic location on the anatomy of the body. The eyelid, for instance, has the thinnest layer of the epidermis, measure but 0.1 mm, whereas the thickest stratum layer, measure approximately 1.5mm.The dermis is thickest on overlying epidermis, wherever it's 30–40 times as thick because the suprajacent epidermis [9, 10].

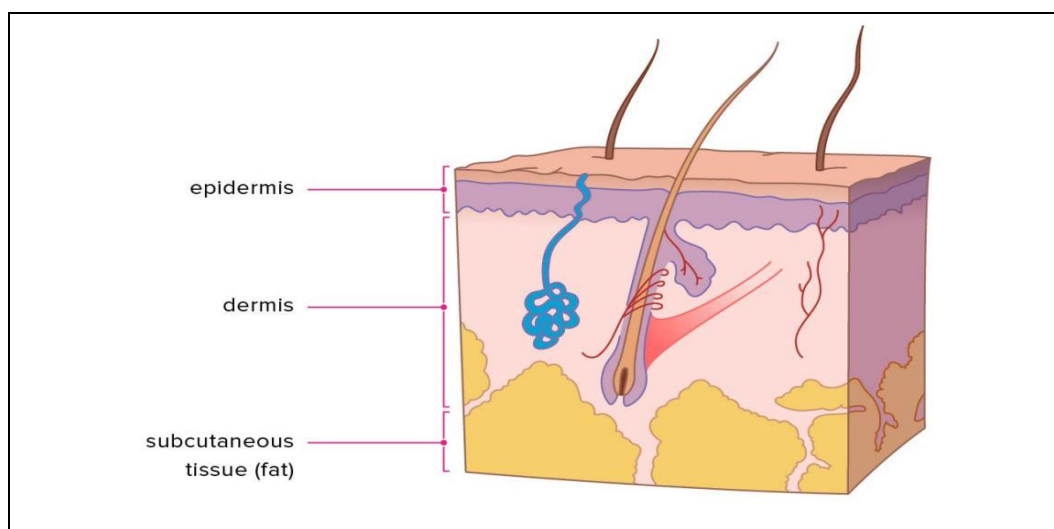


Fig 1: Structure of Skin

Types of skin

1. Epidermis
2. Dermis
3. Subcutaneous

Epidermis

The epidermis is a stratified, squamous epithelium layer that's composed primarily of two varieties of cells: keratinocytes and nerve fibre cells. The keratinocytes differnt from the “clear” nerve fibre cells by possessing intracellular bridges and ample amounts of inclination cytoplasm. [11] The epidermis harbors variety of

alternative cell populations, like melanocytes, Langerhans cells, and Merkel cells, however the keratinocyte cell type contains majority of the cells by far. The cuticle normally is split into four layers according to keratinocyte morphology and position as they differentiate into attractive cells, including the basal cell layer (stratum germinativum), the epithelial cell layer (stratum spinosum), the granular cell layer (stratum granulosum), and also the cornified or attractive cell layer (stratum corneum). The lower three layers that represent the living, cell organ cells of the epidermis are typically observed because the stratum malpighii and structure histologist^[11,12]. The epidermis may be a frequently renewing layer and provides rise to by-product structures, like pilosebaceous apparatuses, nails, and sweat glands. The basal cells of the epidermis undergo proliferation cycles that give for the renewal of the outer epidermis. The epidermis may be a dynamic tissue within which cells are constantly in unsynchronised motion, as differing individual cell populations pass not only one another also conjointly melanocytes and Langerhans cells as they move toward the surface of the skin.^[13]

Dermis

The dermis is an integrated system of fibrous, thin, and amorphous connective tissue that accommodates stimulus-induced entry by nerve and vascular networks, epidermally derived appendages, fibroblasts, macrophages, and mast cells. Different blood-borne cells, as well as lymphocytes, plasma cells, and different leukocytes, enter the corium in response to various stimuli also. The dermis includes the majority of the skin and provides its pliability, elasticity, and strength.^[14] It protects the body from mechanical injury, binds water, aids in thermal regulation, and includes receptors of sensory stimuli. The dermis interacts with the epidermis in maintaining the properties of each tissues. The two regions collaborate throughout development within the development of the dermal-epidermal junction and epidermal appendages and interact in repairing and transforming the skin as wounds are recovered. The dermis doesn't undergo a clear sequence of differentiation that parallels epidermal differentiation; however the structure and organization of the connective tissue elements are predictable in a depth-dependent manner. The matrix elements, as well as collagen and elastic connective tissue, also vary in a depth-dependent manner and undergo turnover and transforming in traditional skin, in pathologic processes, and in response to external stimuli.^[14,15] The constituents of the dermis are mesodermal in origin aside from nerves, which, like melanocytes, derive from the neural crest. Until the sixth week of fetal life, the dermis is simply a pool of dendritic-shaped cells filled with acid-mucopolysaccharides, That are the precursors of fibroblasts. By the 12th week, fibroblasts are actively synthesizing reticulum fibers, elastic fibers, and scleroprotein. A vascular network develops and fat cells have appeared to a lower place the dermis by the 24th week. Infant dermis consists of tiny collagen bundles, whereas the adult dermis contains thicker bundles of collagen. Several fibroblasts are present within the infant dermis, however few continue adulthood.^[16] The principal element of the dermis is collagen, a fibrous family of proteins with a minimum of fifteen genetically distinct varieties in human skin. a major structural protin for the whole body, collagen is found in tendons, ligaments, the liner of bones, and also the dermis. Collagen is a major stress-resistant material of the skin. Elastic fibers, on the other hand, play a task in maintaining physical property however do very little to resist deformation and tearing of the skin. Collagen fibers exist in a constant state of flux, being degraded by chemical change enzymes known as spare collagenases and replaced by new fibers. Collagen represents 70th of the skin's dry weight.^[17] Fibroblasts integrate the procollagen molecule, a selected volute polypeptide chain. Then, the cell secretes the fibroblasts, and they assemble into collagen fibrils. The amino acids glycine, amino acid, and hydroxylysine extremely enrich collagen. The fibrillar collagens found in the skin comprise the main group and are the most abundant proteins within the body. The main constituent of the dermis is type I collagen. Loosely positioned collagen fibers are found in the process and tissue layer dermis, whereas hefty collagen bundles are noted within the reticulated dermis. Type IV collagen is found within the basement membrane zone, and therefore the major structural component of anchoring fibrils is collagen type VII, that is created primarily by keratinocytes. The elastic fiber differs each structurally and chemically from collagen and consists of two components: supermolecule filaments and scleroprotein, an amorphous protin. The fibroblast fuses elastic fiber to the extracellular matrix of the dermis that consists of glycosaminoglycans. The fibers are fine within the process dermis and coarse in the reticulated dermis. Hyaluronic acid is a minor lemen of the traditional corium however that is the major mucopolysaccharide that accumulates in pathologic states.^[18] The location of the nucleus in the center of the muscle fibre and therefore the absence of striation distinguishes smooth muscle from striated muscle. The muscle fibers of the arrectores pilorum are set within the connective tissue of the upper dermis and are connected to the hair follicle below the fatty glands. They are located at such an angle to the hair follicle that when contracted, the hair follicle is pulled into a vertical position, deforming the skin and causing "gooseflesh". Completely different configurations compose small bundles of smooth muscle of the muscularis of veins and arteries. Glomus bodies are specialised aggregates of smooth muscle found between the arterioles and venules, which exist on the digits and lateral aspects of the palms and soles. They regulate body temperature and shunt blood. Striated or voluntary muscles is found within the skin of the neck as ptyasma and in the skin of the face as muscle of expression. The superficial muscular aponeurotic system is an intricate network of muscle, fascia, and aponeuroses connecting muscles with the elements that they move.^[19]

Subcutaneous

The subcutaneous tissue (from Latin subcutaneous 'beneath the skin'), also referred to as the hypodermis, hypoderm (from Greek 'beneath the skin'), subcutis, superficial fascia, is the lowermost layer of the system in

vertebrates. The types of cells found in the layer are fibroblasts, adipose cells, and macrophages. The subcutaneous tissue is derived from the mesoderm, however in contrast to the dermis, it is not derived from the mesoderm's dermatome region. It consists primarily of loose connective tissue, and contains larger blood vessels and nerves than those found in the dermis. It's a serious site of fat storage within the body. In arthropods, a hypodermis will can an epidermal layer of cells that secretes the chitinous cuticle. The term also refers to a layer of cells lying instantly below the epidermis of plants. ^[19] Embryologically, toward the end of the fifth month fat cells begin to develop within the subcutaneous tissue. These lobules of fat cells or lipocytes are separated by fibrous septa created of large blood vessels and collagen. The panniculus varies in thickness depending on the skin site. Considered an endocrine organ, the subcutaneous tissue provides the body with buoyancy and functions as a storage of energy. Hormone conversion takes place in the panniculus, converting androstenedione into estrone by aromatase. Lipocytes produce leptin, a secretion that regulates body weight by method of the hypothalamus. cell proliferation in the epidermis and in epithelial tissue in general and the fact that this tissue is most frequently exposed to physical and chemical injury lead to the exceedingly high rate of skin cancers found in humans as compared with different forms of cancer. ^[20]

Function of Skin ^[21]

Skin performs the following functions:

a. Protection

An anatomical barrier from pathogens and damage between the internal and external environment in bodily defence, Langerhans cells in the skin are part of the adaptive immune system.

b. Sensation

Contains a variety of nerve endings that react to heat and cold, touch, pressure, vibration, and tissue injury, see somatosensory system and haptics.

c. Heat regulation

The skin contains a blood supply far greater than its requirements which allows precise control of energy loss by radiation, convection and conduction. Dilated blood vessels increase perfusion and heat loss, while constricted vessels greatly reduce cutaneous blood flow and conserve heat.

d. Control of evaporation

The skin provides a relatively dry and semi-impermeable barrier to fluid loss. Loss of this function contributes to the massive fluid loss in burns.

e. Aesthetics and communication:

Others see our skin and can assess our mood, physical state and attractiveness.

f. Storage and synthesis

Acts as a storage centre for lipids and water, as well as a means of synthesis of vitamin D by action of UV on certain parts of the skin.

g. Water resistance

The skin acts as a water resistant barrier so essential nutrients aren't washed out of the body.

Advantages & disadvantages:

Advantages ^[22]

Advantages and Disadvantages of cream as a topical drug delivery system.

- It is the easiest way to deliver a drug.
- It does not show the side effect on the other body organ.
- Convenient and easy to apply.
- It does not show the side effect on the other body organ.
- It can slow down the signs of aging.
- Less greasy compared to ointment.

Disadvantages ^[22]

- Skin irritation
- Some drugs show low penetrable through the skin.
- Possibility of allergic reactions.
- Stability is not as good as ointment.
- They are less hydrophobic than other semisolid preparation, so risk of contamination is high than others.

Types of Skin Creams ^[23-25]

They are divided into two types

1. 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.

2. 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.

Classification of Creams ^[26]

A. 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.

B. 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 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 ^[26]

▪ 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.^[27]

4. All-purpose creams and general creams

This creams are used more nowadays type of These creams are somewhat oily but non-greasy 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 body 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. ^[28]

General ingredients used in skin creams

The raw materials which are used in a manufacturing of skin creams include:

Water: This is the most important and widely used raw material in any cream formulation. These are the cheapest and easily available. In skin creams, water is used as solvent to dissolve other ingredients of creams. Water can also form emulsions, it depends upon how much quantity of water is used in the formulation and sometimes referred to as oil-in-water emulsions and sometimes water-in-oil emulsions depending upon the quantities of oil phase and water phase used. ^[29]

Oil, fates and waxes: Oil, fats and waxes and derivatives their form comprise an essential portion of creams. Waxes act as an emulsifier, fats act as a thickener and oil act as a perfuming agent, preservative, etc. according to its function .Oil may be two types' mineral and glyceride

Mineral oil: Mineral oil consists of hydrocarbons derived from petroleum oil .Mineral oil is clear, odorless, and heavily refined oil and it is widely used in cosmetics. It is light weight and inexpensive, it helps to reduce water loss from the body and keeps body moisturized. A number of mineral oils are used in cream formulation. Examples: Light liquid paraffin, Heavy liquid Paraffin , Liquid petroleum

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

Vegetable oil: Form a barrier on the surface of the skin and slow down the loss of water, helping to maintain plumpness of skin. Vegetable oils may also be used to increase the thickness of the lipid or oil portion of cream or personal care products.E.g. Almond oil, germ oil, avocado oil, sunflower oil etc. ^[30]

Waxes: Which are used in preparation of cream includes beeswax, carnauba wax, ceresin, spermaceti, etc. Waxes are used in cosmetics because it helps to keep an emulsion from separation of oil and liquid components. These waxes also increase the thickness of the lipid portion and sticks on the surface of the skin.

Fats: Different types of fats are used in the preparation of creams. These materials can be obtained from animals, plants 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 acid are lauric, margaric, plamitic, 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, coca butter fat, mutton tallow, lard and beef stearine. ^[31]

Lanolin: It is derived from wool fat of a sheep. Lanolin are of two types- the hydrous lanolin contains between 25%- 30% water. Anhydrous lanolin has point of 38°C-42°C and has a slight odour. These ingredients act as a lubricant on the skin surface, which gives the skin soft and smooth appearance. Lanolin helps to form emulsion and blends well with other substances used in cosmetic and personal care products.

Colours: Before the development of the modern technology, colours primarily came from substances found in nature such as turmeric, saffron, indigo, etc. They also could be produced without using plants harvested in the wild. ^[32]

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. ^[33]

Humectants: These are important multi-functional ingredients found in most skin care formulations. Humectants are hygroscopic organic compounds. These are the materials that can absorb or retain moisture.

These has many benefits such as moisturization, exfoliation, etc. Examples of humectant are glycerin, Hydroxyethyl urea, betaine, sodium PCA, Sodium-L-Lactate, etc^[34]

Perfumes: Perfume is a substance that imparts a scent or order, including a sweet and pleasant smell. Examples of natural perfumes used in creams are- White Blossoms, Rosy Dreams, Orange Blossom^[35]

Vitamins: Vitamins plays an important role in maintaining the physiological function of whole body and the skin. Vitamin A, B, C, E etc. are generally used in formulation of the creams.

Preservatives: The use of preservatives in cosmetics is essential to prevent alteration caused by microorganism and contamination during formulation, shipment, storage and consumer use. Antioxidants can also be used to protect alteration caused by exposure to oxygen. Synthetic preservatives when used in low concentration effectively preserve the products^[36]

7. Method of preparation^[37]

1. 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 water-soluble 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.

2. 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.

Evaluation Parameters of Creams^[36-38].

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,

$$S = m \cdot l / t$$

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'.

$$\text{Saponification value} = (b-a) \cdot 28.05 / w$$

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 colour appears after shaking for 30 seconds.

$$\text{Acid value} = n \cdot 5.61 / w$$

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. After feel

Emolliency, 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 lefthand dorsal surface. The cream was applied to the specified area and time was noted. Irritancy, erythema, edema was checked, if any, for regular intervals upto 24hrs and reported.

13. Accelerated Stability Study:

Accelerated stability study is conducted for formulation according to ICH guidelines.^[38]

Applications^[39-41].

1. Skin softening:
2. Smoothing
3. Cooling
4. Moisturizing
5. Anti-allergic
6. Antiseptic
7. Humectant
8. Astringent
9. Cleaning
10. Protective
11. Scabicial
12. Local anesthetic
13. Paraciticide
14. Germicide
15. Antifungal
16. Fairness
17. Antiaging

Conclusion

Creams are semisolid formulations widely acceptable by the society. 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. 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. More advanced technologies and methods will be used for preparation. Formulation and evaluation of creams in coming years.

Reference

1. Sahu T, Patel T, Sahu, Gidwani B. "Skin Cream as Topical Drug Delivery System: A Review" Journal of Pharmaceutical and Biological Sciences, Published by Atom and Cell Publishers. ISSN: 2320-1924
2. James WD, Berger TG, Elston DM, Andrews' Diseases of the Skin: Clinical Dermatology. (10th ed.) Philadelphia; Elsevier Saunders, 2006, 1.

3. Ansel HC, Popovich NG, Allen LV. *Pharmaceutical dosage forms and drug delivery systems*. Lippincott Williams & Wilkins, 1995, 157
4. Rai R, Poudyal AP, Das. *Pharmaceutical Creams and their use in wound healing: A Review*, *Journal of Drug Delivery and Therapeutics*,2019;9(3-1):907
5. Sahu T, Patel T, Sahu S, Gidwani B. *Skin cream as Topical Drug Delivery System: A Review"* *Journal of Pharmaceutical and Biological Sciences*,2016;4(5):149-154
6. Oakley A, Hamilton, *Dermatologist, topical formulation, dormant NZ*.
7. Rai P, Proudly AP, Das S, *Pharmaceutical Creams and their use in wound healing: A Review*, from *Journal of Drug Delivery and Therapeutics*.
8. Chauhan L, Gupta S. *Creams: A Review on Classification, Preparation Methods, Evaluation and its Applications*, *Journal of Drug Delivery and Therapeutics*,2020;10(5-s):281-289
9. James WD, Berger TG, Elston DM. *Andrews' diseases of the skin: Clinical dermatology (10th edition)*. Philadelphia: Elsevier Saunders, 2006.
10. Ross and Wilson. *Anatomy and Physiology in Health and Illness*, 11th
11. Young, Barbara. *Wheater's functional histology a text and colour atlas*. Elsevier, 2014, 160-175.
12. Murphy GF. *Histology of the skin*. In D. Elder, R. Elenitsas, C. Jaworsky, & B. Johnson, Jr. (Eds.), *Lever's histopathology of the skin (8th ed.)*. Philadelphia: Lippincott Williams & Wilkins, 1997, 5-45.
13. Chu DH. *Overview of biology, development, and structure of skin*. In K. Wolff, L.A. Goldsmith, S.I. Katz, B.A. Gilchrist, A.S. Paller, & D.J. Leffell (Eds.), *Fitzpatrick's dermatology in general medicine (7th ed.)*, 2008, 57-73.
14. James William, Berger Timothy, Elston Dirk. *Andrews' Diseases of the Skin: Clinical Dermatology (10th ed.)*. Saunders,2005:1:11-12.
15. Marks James G, Miller Jeffery. *Lookingbill and Marks' Principles of Dermatology (4th ed.)*. Elsevier Inc, 2006, 8-9.
16. Hicklin R. Austin. *"Anatomy of Friction Ridge Skin"*. *Encyclopedia of Biometrics*. Springer US, 2009, 23-28.
17. malvi. *"The Ageing Skin - Part 1 - Structure of Skin and Introduction - Articles"*. *PharmaXChange.info*, 2011.
18. Lin Chang-min et al. *"Microencapsulated human hair dermal papilla cells: a substitute for dermal papilla?"*. *Archives of Dermatological Research*. Springer,2008;300(9):531-535.
19. *Mosby's. Medical, Nursing & Allied Health Dictionary (4th Ed)*. St. Louis: Mosby,1994:998-774.
20. Fischer Josef E, Bland Kirby I, Callery Mark P. *Mastery of Surgery*. Lippincott Williams & Wilkins, 2006, 482.
21. Chauhan Lalita, Gupta Shalini et al, *Journal of Drug Delivery and Therapeutics*,2020;10[5-s]:281-289.
22. Tarun G, Goutam R, and Amit K. *Comprehensive review on additives of topical dosage forms for drug delivery*. *Drug Deliv, Early Online*, 1-1.
23. Kumar KK. *Importance of Critical Quality Attributes in Biopharmaceuticals Development*. *Research Journal of Topical and Cosmetic Sciences*,2019;10(1):29-33.
24. Namjoshi S, Dabbaghi M, Roberts MS, Grice JE, Mohammed Y. *Quality by Design: Development of the Quality Target Product Profile (QTPP) for Semisolid Topical Products*. *Pharmaceutics*,2020;12(3):287.
25. Simões A, Veiga F, Vitorino C, Figueiras A. *A tutorial for developing a topical cream formulation based on the quality by design approach*. *Journal of pharmaceutical sciences*,2018;107(10):2653-62.
26. Paudel KS, Milewski M, Swadley CL, Brogden NK, Ghosh P, Stinchcomb AL. *Challenges and opportunities in dermal/transdermal delivery*. *Ther Deliv*,2010;1(1):109
27. Garg T, Rath G, Goyal AK. *Comprehensive review on additives of topical dosage forms for drug delivery*. *Drug Deliv*,2015;22(8):969-987
28. Billany M. *Suspensions and emulsions*. In: Aulton ME, ed. *Pharmaceutics the Science of Dosage Form Design*. 2nd. Edinburgh, New York: Churchill Livingstone, 2002, 342-357
29. Walters KA, Brain KR. *Topical and transdermal delivery*. In: Gibson M, ed. *Pharmaceutical Preformulation and Formulation: A Practical Guide for Candidate Drug Selection to Commercial Dosage Form*. Boca Raton, FL: CRC Press, 2004, 515-569.
30. Mahalingam R, Li X, Jasti B. *Semisolid Dosages: Ointments, Creams, and Gels*. In: *Pharmaceutical Sciences Encyclopedia: Drug Discovery, Development, and Manufacturing*. Hoboken, NJ: John Wiley & Sons, Inc, 2010
31. Crowley MM. *Solutions, emulsions, suspensions, and extracts*. In: Felton L, ed. *Remington: Essentials of Pharmaceutics*. London, UK: Pharmaceutical Press, 2013, 448-457
32. *International Conference on Harmonization. Q8 ICH. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. ICH Harmonised Tripartite Q8 (R2) Guideline: Pharmaceutical Development*. Geneva, Switzerland: ICH, 2009. Availableat: http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q8_R1/Step4/Q8_R2_Guideline.pdf. Accessed July 17, 2018
33. Aswal A, Kalra M, Rout A. *Preparation and evaluation of polyherbal cosmetic cream* *Der Pharmacia Lettre*,2013;5(1):838

34. Pratikcha R, Adarsh P, Sujit Das, Pharmaceutical Creams and their use in wound healing: A Review, Journal of Drug Delivery & Therapeutics,2019;9(3-s):907-912
35. Bauer JF. Polymorphism—A critical consideration in pharmaceutical development, manufacturing, and stability. J. Valid. Technol,2008:14:15-24
36. Handal S, Hosseini H, Ameri A, Moghimipour E, formulation and evaluation of an antibacterial cream from oxalis corniculata aqueous extract, from jundishapur journal of microbiology.
37. Rai P, Proudly AP, Das S, Pharmaceutical Creams and their use in wound healing: A Review, from Journal of Drug Delivery and Therapeutics.
38. Sahu T, Patel T, Sahu S, Gidwani B. Skin Cream as Topical Drug Delivery System: A Review, from Journal of Pharmaceutical and Biological Sciences.
39. Pal A, Soni M, Patidar K, Formulation and evaluation of polyherbal cream, from International Journal Pharmaceutical and Biological Archives,2014:5:67-71.
40. Avinash G, Priyanka B, Wound healing potential of Indian medicinal plants, from International Journal of Pharmacy Review & Res,2013:2:75-87.
41. Mittal A, Sardana S, Herbal boon for wounds, from International Journal of Pharmacy and Pharmaceutical Sciences,2013:5:1- 12.
42. Pranali S Satkar. A review on pharmaceutical packaging materials. International Journal of Pharmaceutical Science and Research, 2020:5(3):10-13.