A SHORT REVIEW ON NOVEL APPROACH OF CREAM

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ABSTRACT
A cream is a topical preparation usually for application to the skin. Creams for
application to mucus membranes such as those of the rectum or vagina are also used.
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 situation (dermatoses). The use of the Finger tip unit concept may be
helpful in guiding how much topical cream is necessary to cover different areas. Creams
are semi-solid emulsions, that is mixtures of oil and water. 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 water-in-oil (W/O) creams which are composed of small
droplets of water dispersed in a continuous oily phase. Oil-in-water creams are more
comfortable and cosmetically suitable as they are less greasy and more easily washed off
using water. Water-in-oil creams are more difficult to handle but many drugs which are
integrated into creams are hydrophobic and will be released more readily from a water-
in-oil cream than an oil-in-water cream. Water-in-oil creams are also more moisturising
as they provide an oily barrier which reduces water loss from the stratum corneum, the
outermost layer of the skin. Creams can be used for administering drugs via the vaginal
route. Creams are used to help sun burns Composition: There are four main ingredients of
the cream 1: Water 2: Oil 3: Emulsifier 4: Thickening agent

Keywords: Cream, Topical Application.

INTRODUCTION
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. Creams are semisolid dosage forms containing one or more drug substances
dissolved or dispersed in a suitable base. This term has conventionally been applied to
semisolids that possess a relatively fluid consistency formulated as either water-in-oil
(e.g., Cold Cream) or oil-in-water (e.g., Fluocinolone Acetonide Cream) emulsions. However, more recently the term has been limited to products consisting of oil-in-water emulsions or aqueous microcrystalline dispersions of long-chain fatty acids or alcohols that are water washable and more cosmetically and aesthetically acceptable. $^{[1,5]}$

Advantages:-

- Avoidance of first pass metabolism
- Convenient and easy to apply
- Avoid of possibility
- Inconveniences of intravenous therapy and of the varied conditions of absorption like pH changes presence of enzymes gastric emptying time etc.
- Reaching of efficacy with lower total daily dosage of drug by continuous drug input
- Avoid fluctuation of drug levels inter-and intra patent variations$^{[3,42]}$

Disadvantages:-

- Skin irritation of contact dermatitis may occur due to the drug and / excipients
- Poor permeability of some drugs through the skin
- Risk of allergic reactions
- Can be used only for drugs which require very small plasma concentration for action
- Enzyme in epidermis may denature the drugs
- Drugs of larger particle size not easy to absorb through the skin$^{[3,4]}$

General Consideration

The skin anatomy and physiology constrain the parameters to be considered in development of semi-solid dosage forms$^{[1]}$.

Structure and Function of Normal Skin:-

The skin is one of the heaviest body organs and has a surface area of about 2 sqm in an adult.

The skin has several important physiological functions, including:

- Regulation of body temperature
- Protection from external stimuli like chemicals, light, heat, cold and radiation
- Excretion (via sweat glands)
- Synthesis of vitamin D (important in calcium metabolism).
- Containment of body fluids and tissues.
- Response of stimuli like pressure, heat, pain etc.
- Prevent penetration of toxic foreign material & radiation.
- Cushions against mechanical shock.

An individual's skin ranges in thickness from 0.5 mm to 4 mm and consists of two main layers\cite{26,18,39}:

- **Epidermis**:- The thinner outer layer, which is made up of different layers.
- **Dermis**:- The thicker inner layer containing nerve endings, glands, blood vessels, hair follicles and other structures. below the dermis is the fatty subcutaneous layer, which attaches to underlying tissues and organs.

![Figure 1 Layers of Skin](image)

**A. Epidermis:**

The epidermis contains four main types of cell in order in a layered structure known as stratified squamous epithelium. About 90% of cells in the epidermis are keratinocytes. These cells create keratin, a protein that helps water-resistant and defend the skin, and that forms hair and nails. Other epidermal cells include:

- Melanocytes, which generate the pigment melanin
- Langerhans cells, which are involved in immune protection
Merkel cells, which are thought to be involved in the feeling of touch\cite{12,13,12,39}.

Layers of Epidermis:

![Layers of the Epidermis](image)

**Figure 2 Layers of the Epidermis**

**Stratum germinativum:** Basal cells are nucleated, columnar. Cells of this layer have high mitotic index and constantly renew the epidermis and this proliferation in healthy skin balances the loss of dead horny cells from the skin surface\cite{12,14,34}.

**Stratum basale:** The basal cell also include melanocytes which produce the distribute melanin granules to the keratinocytes required for pigmentation a protective measure against radiation\cite{21,20,31}.

**Stratum spinosum:** The cell of this layer is produced by morphological and histochemical alteration of the cells basal layers as they moved upward. The cells flatten and their nuclei reduce in size. They are interconnected by fine prickles and form intercellular bridge the desmosomes. These links maintain the integrity of the epidermis\cite{4,10,33}.

**Stratum granulosum:** This layer is above the keratinocytes. They manufacturing basic staining particle, the keratinohylline granules. This keratogenous or transitional zone is a region of intense biochemical activity and morphological change\cite{21,28,35,38}.

**Stratum lucidum:** In the palm of the hand and sole of the foot, and zone forms a thin, translucent layer immediately above the granule layer. The cells are non-nuclear\cite{27,29,30}.

**Stratum corneum:** At the final stage of differentiation, epidermal cell construct the most superficial layer of epidermis, stratum corneum. At friction surface of the body like
palms and soles adapt for weight bearing and membranous stratum corneum over the remainder of the body is elastic but impermeable. The horny pads (sole and palm) are at least 40 times thicker than the membranous horny layer\textsuperscript{[12,15,18]}.

**Keratinisation:**

The deepest layer is called the stratum basale, which contains the stem cells that produce keratinocytes. The young keratinocytes push upwards through the stratum spinosum, to the stratum granulosum and stratum corneum in a process known as keratinisation\textsuperscript{[3,7,9,17]}.

![Figure 3 Processes of Keratinisation](image)

Keratin is incorporated into the keratinocytes in the stratum granulosum and, as their nuclei degenerate, the keratinocytes die. When they reach the stratum corneum, the keratinocytes have flattened and are completely filled with keratin. Eventually they are sloughed off, to be replaced by the next row of keratinocytes. The whole process of keratinisation takes approximately 2-4 weeks\textsuperscript{[16,26,39]}.

**B. Dermis:-**
Non-descriptive region lying in between the epidermis and the subcutaneous fatty region. It consist mainly of the dense network of structural protein fibre i.e. collagen, reticulum and elastin, embedded in the semi gel matrix of mucopolysaccaridic 'ground substance'. The elasticity of skin is due to the network or gel structure of the cells. Protein synthesis is a key factor in dermal metabolism.

The dermis is composed of connective tissue containing blood vessels, collagen and elastin fibres with a few fat cells, macrophages and fibroblasts interspersed. It also contains specialised nerve endings that are sensitive to touch (Meissner's corpuscles), pressure (Pacinian corpuscles), heat and cold. Sweat glands, sebaceous glands and hair follicles are embedded in the dermis and extend through the epidermis to open onto the surface of the skin. A pilosebaceous follicle is a unit consisting of one hair and an associated sebaceous gland\[^{2,8,14,15,19}\].

**Pilosebaceous Follicle:-**

There are three kinds of pilosebaceous follicle in the dermis:

1. Vellus follicles, comprising a tiny hair and a much larger sebaceous gland.
2. Sebaceous follicles, comprising a tiny hair and an exceptionally large multiacinar sebaceous gland.
3. Terminal hair follicles, comprising a long, stiff, thick hair and a proportionately sized sebaceous gland.
The sebaceous follicles are the only ones involved in acne, although the other types contribute to the amount of lipid on the surface of the skin. Sebaceous follicles are found only on the face, upper arms, chest and upper back, and acne vulgaris can only occur in these areas. Sebaceous glands throughout the body, including those in the sebaceous follicles, produce sebum, an oily substance consisting of a mixture of fats, cholesterol, proteins and salts. Sebum spreads from the sebaceous follicle onto the hair and skin. It prevents hair from drying out and keeps skin supple. It also inhibits the growth of certain bacteria\(^{[31,32,37]}\).

1. **Subcutaneous Tissue:**

   This layer consists of sheet of fat rich areolar tissue; known as superficial fascia, attaching the dermis to the underlying structure. Large arteries and vein are present only in the superficial region\(^{[33,37,39]}\).

2. **Skin Appendages:**

   The skin is interspersed with hair follicle and associated sebaceous gland like two types of sweat glands eccrine and apocrine. Collectively these are referred as skin appendages\(^{[33,35,39]}\).

3 Absorption through Skin:- \(^{39-41}\)

   Two principal absorption routes are identified:
   - Transepidermal Absorption
   - Transfollicular Absorption

**Transepidermal Absorption:**

   It is now generally believed that the transepidermal pathway is principally responsible for diffusion across the skin. The resistance encountered along this pathway arises in the stratum corneum. Permeation by the transepidermal route first involves partitioning into the stratum corneum. Diffusion then takes place across this tissue. The current popular belief is that most substances diffuse across the stratum corneum via the intercellular lipoidal route. This is a tortuous pathway of limited fractional volume and even more limited productive fractional area in the plane of diffusion. However, there appears to be another microscopic path through the stratum corneum for extremely polar compounds and ions. Otherwise, these would not permeate at rates that are measurable considering their o/w distributing tendencies. When a permeating drug exits at the
stratum corneum, it enters the wet cell mass of the epidermis and since the epidermis has no direct blood supply, the drug is forced to diffuse across it to reach the vasculature immediately beneath. The viable epidermis is considered as a single field of diffusion in models. The epidermal cell membranes are tightly joined and there is little to no intercellular space for ions and polar nonelectrolyte molecules to diffusively squeeze through. Thus, permeation requires frequent crossings of cell membranes, each crossing being a thermodynamically prohibitive event for such water-soluble species. Extremely lipophilic molecules on the other hand, are thermodynamically embarrassed from dissolving in the watery regime of the cell (cytoplasm). Thus the viable tissue is rate determining when nonpolar compounds are involved. Passage through the dermal region represents a final hurdle to systemic entry. This is so regardless of whether permeation is transepidermal or by a shunt route. Permeation through the dermis is through the interlocking channels of the ground substance. Diffusion through the dermis is facile and without molecular selectivity since gaps between the collagen fibers are far too wide to filter large molecules. Since the viable epidermis and dermis lack measure physiochemical difference, they are generally considered as a single field of diffusion, except when penetrants of extreme polarity are involved, as the epidermis offers measurable resistance to such species[22,27,28].

Transfollicular (Shunt Pathway) Absorption:-

The skin’s appendages offer only secondary avenues for permeation. Sebaceous and eccrine glands are the only appendages, which are seriously considered as shunts bypassing the stratum corneum since these are distributed over the entire body. Though eccrine glands are numerous, their orifices are tiny and add up to a miniscule fraction of the body’s surface. Moreover, they are either evacuated or so copiously active that molecule cannot diffuse inwardly against the glands output. For these reasons, they are not considered as a serious route for percutaneous absorption. However, the follicular route remains an important avenue for percutaneous absorption since the opening of the follicular pore, where the hair shaft exits the skin, is relatively large and sebum aids in diffusion of penetrants. Partitioning into sebum, envisioned mechanism of permeation by this route. Vasculature sub serving the hair follicle located in the dermis is the likely point of systemic entry. Absorption across a membrane, the current or flux is and terms
of matter or molecules rather than electrons, and the driving force is a concentration gradient (technically, a chemical potential gradient) rather than a voltage drop. A membranes act as a “diffusional resistor.” Resistance is proportional to thickness (h), inversely proportional to the diffusive mobility of matter within the membrane or to the diffusion coefficient (D), inversely proportional to the limited area of a route where there is more than one (F), and inversely proportional to the carrying capacity of a phase\[^{23,24,36}\].

\[ R = \frac{h}{FDK} \]

Where \( R \) =Resistance of diffusion resistor

- \( F \) = Fractional area
- \( h \) = Thickness
- \( D \) = diffusivity
- \( K \) = Relative capacity

4 Basic Principle of Permeation: \[^{39-41}\]

In the initial transient diffusion stage, drug molecule may penetrate the skin along the hair follicles or sweat ducts and then be absorbed through the follicular epithelium and sebaceous glands. When a steady state has been reached diffusion through stratum corneum becomes the dominant pathway. The membrane-limited flux (\( J \)) under steady condition is described by expression\[^{25,28,30}\].

\[ J = \frac{DAK_{w/o} \Delta C}{h} \]

Where:

- \( J \) = Amount of drug passing through the membrane system per unit area per unit time.
- \( D \) = Diffusion coefficient
- \( A \) = Area of the membrane
- \( C \) = Concentration gradient
- \( K_{w/o} \) = Partition coefficient
- \( h \) = Thickness of the membrane
Figure 5 Schemes of Events for Percutaneous Absorption

1. Dissolution of drug in vehicle
   - Dissolution of drug through vehicle to skin surface
   - **TRANSEPIDERMAL ROUTE**
     - Portioning into Stratum Corneum
     - Diffusion through protein-lipid matrix of Stratum Corneum
     - Partitioning into viable Epidermis
     - Diffusion through cellular mass of Epidermis
     - Diffusion through cellular mass of upper Epidermis
     - Capillary uptake and systemic dilution
   - **TRANSFOLLICULAR ROUTE**
     - Portioning into Sebum
     - Diffusion through lipids in Sebaceous Pore
Factor Affecting Topical Permeation:

Physicochemical properties of drug substances are as follows[26,25,29]:

- Partition coefficient
- pH-condition
- Drug solubility
- Concentration
- Particle size
- Polymorphism
- Molecular weight

Kinetics of Permeation:

Knowledge of skin permeation is vital to the successful development of topical formulation. Permeation of a drug involves the following steps[32,36,39]-

1. Sorption by stratum corneum
2. Penetration of drug through viable epidermis
3. Uptake of the drug by the capillary network in the dermal papillary layer

This permeation can be possible only if the drug possesses certain physicochemical properties. The rate of permeation across the skin \( \frac{dQ}{dt} \) is given by equation. (1)

\[
\frac{dQ}{dt} = P_s(C_d - C_r)
\]  \hspace{1cm} (1)

Where \( C_d \) and \( C_r \) are, the concentrations of skin penetrant in the donor compartment (e.g. on the surface of stratum corneum) and in the receptor compartment (e.g., body) respectively. \( P_s \) is the overall permeability coefficient of the skin tissues to the penetrant. This permeability coefficient is given by the relationship:

\[
P_s = \frac{K_s D_{ss}}{H_s}
\]

Where \( K_s \) is the partition coefficient for the interfacial partitioning of the penetrant molecule from a solution medium on to the stratum corneum, \( D_{ss} \) is the apparent diffusivity for the steady state diffusion of the penetrant molecule through a thickness of skin tissues and \( H_s \) is the overall thickness of skin tissues. As \( K_s \), \( D_{ss} \) and \( H_s \) are
constant under given conditions, the permeability coefficient ($P_s$) for a skin penetrant can be considered to be constant\cite{31,37,38}.

From equation (1) it is clear that a constant rate of drug permeation can be obtain when $C_d >> C_r$ i.e. the drug concentration at the surface of the stratum corneum ($C_d$) is consistently and substantially greater than the drug concentration in the body ($C_r$) and the rate of skin permeation ($dQ/dt$) is constant provided the magnitude of $C_d$ remains fairly constant throughout the course of skin permeation. For keeping $C_d$ constant, the drug should be released from the device at a rate ($R_r$) that is either constant or greater than the rate of skin uptake ($R_a$) i.e. $R_r >> R_a$.

Chemical Penetration Enhancer:

By definition, a chemical skin penetration enhancer increases skin permeability by reversibly destructive or by altering the physicochemical nature of the stratum corneum to reduce its diffusional resistance. Among the alterations are increased hydration of stratum corneum and/or a change in the structure of the lipids and lipoproteins in the intercellular channels through solvent action or denaturation. These may conveniently be classified under the following main heading\cite{22,33,37}:

\[\text{Ø Solvents:}\] These compounds increase penetration possibly by swelling the polar pathway and/or by fluidizing lipids. Example include water, methanol and ethanol; alkyl methyl sulfoxide, dimethyl sulfoxide, dimethyl acetamide and dimethylformamide; pyrrolidone- 2 -pyrrolidone, N-methyl, 2- pyrrolidone; laurocapram (Azone), miscellaneous solvents- propylene glycol, glycerol, silicone fluids, isopropyl palmitate.

\[\text{Ø Surfactant:}\] These compounds are proposed to enhance polar pathway transport, especially of hydrophilic drugs. The ability of the surfactant to alter penetration is a function of polar head group and the hydrocarbon chain length. Commonly used surfactant are as follows:

a) **Anionic surfactant:** It can penetrant and interact strongly with skin. Example includes Dioctyl sulphosuccinate, Sodium lauryl sulphate, Decodecylmethyl sulphoxide etc.

b) **Cationic surfactant:** Cationic surfactants are reportedly more irritating than anionic surfactants and they have not been widely studied as skin permeation enhancer.
c) Nonionic surfactant: Nonionic surfactants have least potential for irritation. Example includes Pluronic F127, Pluronic F68 etc.

d) Bile salts: Sodium taurocholate, Sodium deoxycholate, and Sodium tauroglycocholate.

e) Binary system: These systems apparently open the heterogeneous multilaminated pathway as well as the continuous pathways. Example includes Propylene glycol, oleic acid and 1, 4-butane diol-linoleic acid.

f) Miscellaneous chemicals: These includes urea, N, N-dimethyl-m-toluamide, calcium thioglycolate etc[32,34,33].

5. Physicochemical Properties of Topical Products:

a) Release characteristics:- The mechanism of drug release depends on whether the drug molecules are dissolved or suspended in the delivery system. The interfacial partition coefficient of drug from delivery systems to the skin pH of the vehicle

b) Composition of drug delivery system:- Example polyethylene glycols of low molecular weight decrease permeation.

c) Nature of vehicle:- Lipophilic vehicle increase permeation where as lipophobic vehicle decrease permeation[23,29,31].

Topical Dosage Forms:-
Topical dosage forms are applied externally and used to deliver the drug across a localized area of the skin. To develop and ideal topical dosage form one must consider the factors like:

1. Flux of drug across skin.
2. Retention of the dosage form on skin surface.
3. Reservoir capacity of the dosage form
4. Patient’s suitability[22,27,32].

Types of Topical Dosage Forms:-
Main topical dosage forms are:

1. Ointment
2. Cream
3. Gel
4. Lotion
5. Solution

**CREAMS:**
These are the solid or semisolid preparation which is either an o/w or w/o type emulsion. Creams are preferred to ointment because they are easier to spread and in case of o/w emulsion they are easier to remove. Today, the use of cream cosmetics products has increased tremendously. Human contact to cosmetics formulations and their ingredients occurs primarily via the topical route such as cream and lotion. Several considerations are necessary regarding the appropriateness and safety of cosmetics, because cosmetics preparations are used nearly continually and in direct contact with the skin\[^{33,34,38}\].

**W/O Creams:**
These types of creams contain water dispersed in oil phase with help of emulsifier. This type of cream is chosen to ointment because as the water evaporates from the skin the process soothes the inflamed tissue\[^{33,35,38}\].

**O/W Creams:**
O/W creams generally rub into the skin and disappear with little or no trace of their former presence. Hence they are called vanishing creams. On application to skin much of the continuous phase evaporates and increases the concentration of water soluble drug in adhering film. The concentration gradient for drug across the stratum corneum should therefore increase and promote percutaneous absorption. To minimize drug precipitation and to promote drug bio-availability water miscible co-solvent such as propylene glycols, glycerine, ethanol, polyethylene glycols may be incorporated. O/W creams are non occlusive because they do not deposit a continuous film of water imperious lipid. A correctly formulated cream can deposit lipids and other moisturizer on and in stratum corneum and reinstate the tissue ability to hydrates. Creams are semisolid emulsion system that has a creamy appearance as the result of reflection of light from their emulsified phase\[^{36,38,39}\].

**Types of creams:**
- A. Cleansing cream
- B. Massage creams
- C. Night creams
- D. Moisturizing creams
E. Foundation creams
F. Vanishing creams
G. All purpose creams

A. Cleansing cream:-

Cleansing cream is required for removal of facial make up, surface grime, oil, water and oil soluble soil efficiently mainly from the face & throat\textsuperscript{[34,44,38]}. 

Characteristic of a good cleansing cream:-

1. Be able to effectively remove oil soluble & water soluble soil, surface oil from skin.
2. Should be stable & have good appearance.
3. Should melt or soften on application to the skin
5. Its physical action on skin & pore openings should be that of flushing rather than absorption\textsuperscript{[5,819]}.

Type of cleansing cream:-

I.) Anhydrous type:-

It contains mixture of hydrocarbon, oils and waxes. It also contains cetyl alcohol, spermaceti, cocoa butter, fatty acid esters etc. Not popular\textsuperscript{[35,37,39]}.

Mineral oil………………………..80 gm,
Petroleum jelly…………………..15gm
Ozokerite wax ……………………5 gm
Preservative and perfumes ………q.s

Note: - Formation crusty surface is avoided by adding Ozokerite & petrolatum (prevent bleeding of mineral oils.) Opaque character obtained by adding Zno, mg.stearate, Tio2

II.) Emulsified type:-

They can be either o/w or w/o type.

Common Ingredients:-

Oil phase.........................Spread easily
Waxes.........................Give appropriate thixotropy
Emollient material.................likes cetyl alcohol, spermaceti, and lanolin
Water phase with preservative
Different types:-

Cold Cream:-
Cooling effect is produced due to slow evaporation of the water contained in the formulation. These are w/o type\textsuperscript{[32,34,39]}.

Beeswax Borax type:-
These contain high percentage of mineral oil. These are o/w type. This cream contains high amount of mineral oil for cleansing action. Basically these are o/w type emulsion. After the cream is being rubbed into the skin satisfactory quantity of water evaporates to impart a phase inversion to the w/o type. The solvent action of the oil as external phase imparts cleansing property. In this type of cream borax reacts with free fatty acids present in the bees wax and produces soft soap which acts as the emulsifying agent and emulsifies the oil phase\textsuperscript{[27,29,38]}.

A typical formulation:-
Bees wax ……………………….2 gm
Borax…………………………….2 gm
Almond oil………………………50 gm
Rose water ………………………35.5 gm
Lanolin………………………….. 0.5gm
Preservative and perfume ……….q.s

B) Night & massage cream:-
These are generally applied on the skin and left for several hours say overnight and assist in the revamp of skin which has been injured by exposure to various elements or exposure to detergent solution or soap. The mostly have a moisturizing & a nourishing effect of affected skin. These also contain vitamins and hormones basing on the application. This cream gives better look to the skin and prevents dryness.\textsuperscript{[6,9,8]}

A typical formulation
Mineral oil………………….38gm
Borax …………………….1gm
Petroleum jelly………………8gm
Water …………………….35gm
White bees wax…………….15gm
Perfume & preservative…… q.s
Paraffin wax ………………1.0gm
Lanolin…………………… 2gm

C) Vanishing cream:-
These are named so as they seem to vanish when applied to the skin. High quantity of stearic acid as oil phase use. This provides an oil phase which melts above body temperature and crystallises in a suitable form, so as to imperceptible in use and gives a non greasy film.

- Main component is emollient esters ,stearic acids
- Part of stearic acid is saponified with an alkali & rest of stearic acid is emulsified this soap in big quantity of water.
- The quality of cream depends on the amount of acid saponified & nature of alkali used.
- NaOH makes harder cream than KOH.
- Borax makes cream very white but product has tendency to grain.
- Pearliness can be attained using liq.paraffin, cocoa butter, starch, castor oil, almond oil.
- Ammonia solution has a tendency to discolor creams made with it after some time.
- Cetyl alcohol improves touch and stability at low temperature without affecting sheen[6,8,11].

A typical formulation
Stearic acid………………15gm
Glycerin………………… 5gm
KOH…………………….. 0.5 gm
Water…………………….. 75.82 gm
NaOH…………………….. 0.18 gm
Cetyl alcohol……………... 0.50 gm
Propylene glycol…………...3.0gm
Preservative &perfume……..q.s

Stearic acid has whiteness like snow so some times the preparation is called as SNOW.
D) Foundation cream:-
They are applied to skin to provide a smooth emollient base or foundation for the application of face powder & other make up preparations. They help the powder to adhere to skin. They are almost o/w type[^33,26,38].

Types:
1) Pigmented
2) Unpigmented

A typical formulation
- Lanolin………………………… 2 gm
- Propylene glycol ………………...8gm
- Cetyl alcohol……………………. 0.50 gm
- Water ................................. 79.10 gm
- Stearic acid ..............................10gm
- Perfume & preservative.............q.s
- KoH....................................... 0.40 gm

E) Hand & body cream:-
- The repeated or constant contact with soap and detergent damages & removes film of sebum thus this cream is used to impart following functions to the skin.
- The function of these creams are
  - reduce water loss.
  - Provide oily film to protect the skin.
  - Keep the skin soft, smooth but not greasy.

Type: - a) Liquid cream:- consistency is of liquid nature
  b) Solid creams: - Consistency is higher
  c) Nonaqueous type:- Not containing any aqueous medium[^22,27,29].

A typical formulation
a.) Isopropyl myristate ....... 4 gm
   Mineral oil .......................2 gm
   Stearic acid .....................3 gm
Emulsifying wax …………0.275 gm
Lanolin ……………………2.5 gm

b.) Glycerin …………………3.0 gm
Triethanolamine ………..1 g
Water ………………………84.225 gm
Perfume and Preservative …q.s

(F) All purpose creams:-
All purpose means it is suitable for hands, face and body. They are w/o types\textsuperscript{[9,11,17]}. Formula:-

For oil phase
Mineral oil 18%
Petroleum jelly 2%
Paraffin wax 3%
Ozokerite 7%

For water phase
Water 61.3%
Glycerol 5%
Magnesium sulphate 0.2%
Perfume, preservative q.s

Evaluation of cream
As per the requirements for skin creams specified, following parameters are used for evaluation of cream\textsuperscript{[21,24,34]}.

Thermal stability
For thermal stability testing, a humidity chamber and clear glass container of around 30ml capacities with screw cap are used. With the help of spatula cream is inserted in the glass containers and tapped to settle to the bottom and plug is inserted and tightens the cap. The packed bottle is kept inside the incubator at 45\textdegree\ C for 48h. On removal from the incubator, it is noted that no oil separation or any other phase separation will not observed, than formulated cream is stable at 45\textdegree\ C\textsuperscript{[21,24,31]}.

Determination of pH of formulated Cream:-
The digital pH meter is calibrated using buffer solution of pH 4.01, 7.0 and 9.2. Cream is taken in a beaker and the pH of the cream is determined.[30,31,31]

Appearance:
The appearance of the cream is judged by its color, pearlescence and roughness and graded.[22,26,28]

After feel:
Emolliency, slipperiness and amount of residue left after the application of fixed amount of cream is check.[29,27,38]

Type of smear:
After application of cream, the type of film or smear formed on the skin are check.[24]

Removal:
The ease of removal of the cream applied is examined by washing the applied part with tap water.[24]

Acid value:
Take 10 gm of substance dissolved in accurately weighed, in 50 ml mixture of equal volume of alcohol and solvent ether, the flask is joined to reflux condenser and slowly heated, until sample is dissolved completely, to this 1 ml of phenolphthalein added and titrated with 0.1N NaOH, until faintly pink color appears after shaking for 30 seconds.[26,35]

Acid value = n*5.61/w
n = the number of ml of NaOH required.
w = the weigh of substance.

Saponification value:
Introduce about 2 gm of substance refluxed with 25 ml of 0.5 N alcoholic KOH for 30 minutes, to this 1 ml of phenolphthalein added and titrated instantly, with 0.5 N HCl.[28,30,38]

Saponification value = (b-a)*28.05/w
The volume in ml of titrant = a
The volume in ml of titrant =b
The weigh of substance in gm = w

Irritancy test:
Mark an area (1sq.cm) on the left hand dorsal surface. The cream is applied to the specified area and time is noted. Irritancy, erythema, edema, is checked if any for regular intervals up to 24 hrs and reported[^33,^37,^39].

**Determination of total fatty substance content:**

About 2g of the exactly weighed formulated cream is taken into a conical flask. Dilute Hydrochloric acid (25ml) is added and a reflux condenser is fixed into the flask and the solution is boiled until it completely cleared. Then contents of the flask are poured into a 300ml-separating funnel and it is cooled to room temperature. In portion of 10ml the conical flask is rinsed with 50 ml of petroleum ether and poured into the separating funnel, separating funnel is then shaked well and left until the layers are separated. An aqueous phase is separated and all ether extract is then washed with water. This petroleum ether extract is then filtered through a filter paper and dried the material in the flask at a temperature 90 ± 2 °C of to constant mass[^39].

Formula:

\[
\text{Total fatty substance} = 100 \frac{M_1}{M_2}
\]

Where,

- \(M_1\) = mass (g) of the residue
- \(M_2\) = mass (g) of the cream

**Determination of residue:**

About 5g of the cream is taken in a weighed, clean and dry squat form weighing bottle and dried to constant mass at 105 ± 1 °C. Cooled in a desiccator and weighted[^31,^37,^38].

Formula:

\[
\text{Residue} = 100 \frac{M_1}{M_2}
\]

Where,

- \(M_1\) = mass (gm) of the residue
- \(M_2\) = mass (gm) of the cream

**Test for lead:**

Standard lead solution is prepared by using 1.600gm of the lead nitrate taken in water and the solution is made to 1000ml. solution (10ml) is Pipette out and diluted to 1000ml with water. 1 ml of this solution contains 0.01mg of lead (Pb). About 2.00gm of cream is taken in a crucible and heated on a hot plate and then taken in a muffle furnace to ignite it at
600 °C to constant mass. Dilute hydrochloric acid 3ml (5N) is added and warmed and volume is made to 100ml. solution is then filtered. In the second Nessler’s cylinder, 2 ml of dilute acetic acid (1N) is added, volume is made with water to 25ml. standard hydrogen sulphide(10ml) solution is added to each Nessler’s cylinder and volume is made with water (50ml) mixed and allowed to stand for 10min and the colour produced in two Nessler’s cylinders is compared. The colored produced with hydrogen sulphide is matched against that obtained with standard lead solution\textsuperscript{39,39}.

**Spreadability:**

Spreadability of cream is measured with the glass slide apparatus, overkill of cream is placed between two slides and 1 kg weight is placed on slide for 5 min. to compress the sample to uniform thickness, time in seconds to separate two slides is taken as measure of spreadability\textsuperscript{31,34,39}.

\[
S = \frac{w l}{t}
\]

where,

- \(S\) = spreadability (g cm/sec)
- \(w\) = weight on upper slide (g)
- \(l\) = length of Slide (cm)
- \(t\) = time taken in sec (sec)

**Homogeneity:**

The developed cream is tested for homogeneity by visual inspection, after the cream have been set in the container, spread on the glass slide for the appearance, tested for the presence of any lumps, flocculates or aggregates\textsuperscript{33,37,39}.

**Consistency:**

Consistency of the formulation is determined by penetrometer\textsuperscript{32,37,39}.

**Microbial evaluation:**

Microbial evaluation of herbal formulations is essential to check the limits of microbial contamination and extents of pathogenicity. This evaluation has direct correlation with the quality of products. For the evaluation of total microbial count details of different count media are used, nutrient agar medium used for the growth of bacteria and Potato dextrose agar medium is used for the growth of fungi. [15]
In aseptic conditions cream equivalent to 1 gram is dissolved in 10ml of sterile water and is serially diluted. The medium and apparatus required for experimental are sterilized in an autoclave at 121 °C for 15min. In aseptic conditions, 1ml of test sample is transferred to petridish containing melted agar medium at about 42 °C and mixed well by rotating the petridish. It is allowed to solidify and then incubated at 37 °C for 24h for detection of bacteria. After incubation period, colonies are counted.[33,31,39].

Formula:

\[
\text{No. of Microorganism} = \frac{\text{No. of colonies} \times \text{dilution factor}}{\text{Volume of sample}}
\]

Stability testing of formulated cream:-

For assessing the stability of formulated creams following parameters are taken into consideration like Thermal stability testing, pH, Total fatty substance content, Total residue, General test for lead, Consistency, Spreadability. [16] These studies are essential to ensure that product is stable over its designated shelf life. The stability study is carried out for three months as per ICH norms, at three different temperatures such as at room temperature, 45°C and 8 to 10°C [2,14,28].

Salient applications of cream:-

In order to formulate an effective and efficient cream preparation, deliberation must be given to the intended purpose. This is directly concerned with the site of action and the desired effect of the preparation. Cream preparations may be used for [21,34,27]

Surface Effects:-

Cleansing (removal of dirt and germs), Cosmetic (enhancement of appearance), Protective (prevention of moisture loss, sunscreen), Antimicrobial (reduction of infection) [31,32,33].

Stratum Corneum Effects:-

Protective (e.g. sunscreens that penetrate this layer), keratolytic (a sloughing of the skin, useful in the treatment of psoriasis), protective (moisturizing) [26,35,39].

Viable Epidermal and Dermal Effects:-
Several classes of drugs may pierce to these layers (anti-inflammatory, anesthetic, and antipruritic, antihistamine). Although it is difficult for drugs to penetrate the stratum corneum, once they are in the dermis, they can diffuse into the general circulation. It is difficult to formulate a drug with only a local effect without subsequent uptake by the blood\footnote{33,39,40}.

**Systemic Effects:**

A few drugs, such as Scopolamine, Nitroglycerin, Clonidine, and Estradiol, have been formulated in a manner to achieve systemic effects\footnote{35,39}.

**Appendage Effects:**

Some classes of drugs are intended to exert their action in these portions of the skin (depilatory, exfolient, antimicrobial, and antiperspirant)\footnote{25,32,36}.

**REFERENCE**


37. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2700785/figure/F1/