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Review

A brief review on declarative concepts of pharmaceutical characteristics, classification, mechanisms, preparation, formulation and evaluation studies of moisturizing cream

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Abstract: The pharmaceutical creams play important role on tropical applications in which moisturizers are one of the widely industrial preparations involved for to nourish, soften and moisten the skin for the clients. These are mainly effectively works on dry skin clients combating various cases such as itch, pain, stinging, tightness, tingling and many more problems. The moisturizers are products mainly aimed to raising the SC's water surface content helps the skin smooth, hydrates and hence maintaining a normal pH of skin. They are classified as emollients, humectants, occlusives and protein rejuvenators moisturizers helps to aid skin layers and even modifies its barriers. But its ingredients needed to be considered as non-irritant, nontoxic and non-adverse effects. This review main purpose is to describe about the overall published studies being for making moisturizing creams are interest able, advantageous and all the characteristics, mechanism, preparation, formulation and evaluation within the elegant criteria fulfilled. Even have clinical details for various disorder which are already been suggested by expert as well as adjuvant therapy suggested by experts. The patterns are being studied about water-in-oil emulsion design along with its needs which are being qualified under evaluation parameters for to know about qualified moisturizing creams.

Keywords: dry skin clients; moisturizers; characteristics; skin pH; non-irritant; elegant criteria's

1. Background intro of creams with respect to moisturizers

Pharmaceutical cosmetics are those products that are being generally required to beautify the adorable skin and to purify the skin. This word cosmetic derived from Greek word "Kosmesticos" which mean to adorn [1]. Creams are basically defined as though those semisolid emulsions which are under oil in water (O/W) or water in oil (W/O) types where these emulsions are intended for externally applications. Creams were categorized are of two previously known as O/W and W/O where both are beneficial with multiple needs under demand. It must be applying on the outer part or the superficial part of skin with its main ability is to remain a longer time period at the site of application [2].

Moisturizer actually refers to the cosmetic aspect of cream preparation used for moisten, protection and lubrication the skin upper layer and even have its liquid property that being helpful for soften the skin, especially for prepared dry natured skin clients. It enhances the water content by to reduce evaporation which is specifically designed to either impact or restore hydration under skin [3]. They are several varieties of them available in market, but most of the commonly use excipients or the qualified

cream bases are thickening agent, surfactants, emulsifiers, synthetic adhesives, perfuming agents, pigments and many more to get and form of this cream base. There are being extensive need for replacement of toxic, irritant or synthetic agents instead of using naturally derived herbs [4,5].

The main aim of moisturizers function is to develop the herbal cream which can provide multiprotective effects, such as reduced dust, dirt, moisture, pimples, acne, skin irritation and even microbes free to reduce skin roughness or from flaky or dry patches generated during environmental conditions in winter or other such environmental factors and even additional glow to the face [4]. The term "moisturizer" is used frequently interchangeably in despite of emollients or humectants with occlusives with its cream base as commonly included in moisturizers precisely while its purpose is to enhancing the water-binding competency of the Stratum corneum (SC) of the epidermis skin layer. Where, the term 'emollient' inferred with (from the Latin derived) an object designated to soften the skin that 'smoothens' the surface while touching and even its feel makes the surface look smoothen sees satisfying for the looking eyes [5].

These are widely applicable for both oily and dry skin clients by which their preparation helps to enhance the water content under the SC and hence being to bear its vital action, known as moisturizing or moistening action despite to maintain normal skin pH and even allows the bilayers of lipid under skin easier to normalize and re-establishing its capability for connecting corneocytes together allowing from retention of moisture between the intercellular spaces [6]. Substantially, the hydration interrupts the skin cycle by which its surface becomes soft, smooth, and even more protractile. Moisturizers are rarely implying with health related to problems as compared to other prescriptional tropical drugs in respite for being applying on the surface area of the body for long duration. Up to recent studies, we have indicated through various observational data that via by many ingredients shows different characteristics are used including their manufacture [7].

Therefore, in addition to anticipated by many dermatologists suggested that characteristics, such that in spite of aesthetic beauty influencing patient adherence to predicted clinical efficacy by which irritancy and allergic nature that affects subjective feeling, safety and tolerability factors under consideration while preventing unnecessary discomfort [8]. They frequently associated with a variety of discomforts including tightness, stinging and itching and burning sensations, where the overall side effect is related to skin irritation, which described as sensory reactions with or without indications of eczemas or inflammation. In addition, there are few plausible actions make use by moisturizers including anti-inflammatory action by blocking COX action [9].

From ancient times to updated recent data, people are still using polyherbal or herbal cosmetics for the beautifying of skin which gives longer duration of contact time effect at the application site as being differentiated to others semisolid formulations. They provide elegant appearance for the skin which much not that greasy. While in contact with oil phase gives an emollience effect to the skin. The function of moisturizing cream to restore moisture from dry skin and even allows eliminating the pore's waste materials shows cooling effect sensation under body. It is water proof which gets ease to wash away [10].

They are non-conservative and gets liquefy at ease body temperatures under natural pores. They are even commonly helpful to reduce fine lines, smoothen and hydrate the skin which improves patient's social, psychological and quality of healthy being life and hereby the well satisfaction of the treated individual as shown in **Figure 1** [10].

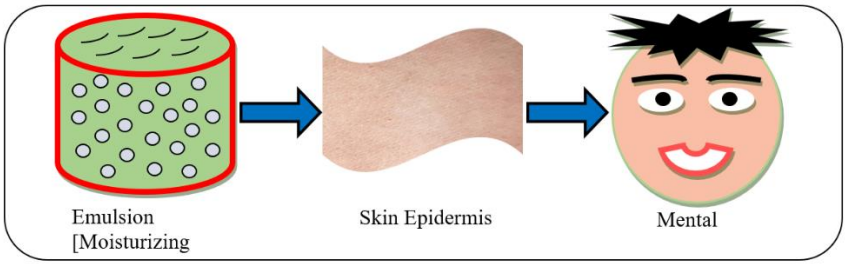

Figure 1. The quality, function and efficiency of cream which influence the social, psychological and quality of healthy being life of skin and hereby the well satisfaction of the treated individual [7].

Moisturizers are apparent treatment for dry skin type with many health care patients and with professionals who overlook its value of needs and declare them not to be "active treatments", even they not realized the SC abnormality which may be the primary factor of the skin diseases [10,11]. Only few clinical studies that are currently controlled, but their scientific addition studies on its mechanism affecting the SC causing the dermatitis considered as non-dispensable. Not only the API, but excipients used under moistures incorporated mainly to improve stability and viscosity mainly implies with the anatomy and physiolosy of skin [12].

2. History of moisturizer cream

Surprisingly previously, as such no agreement/consensus about the fixed define of moisturizers, despite having a deep history. But in term itself which is familiar tense coined by Madison Avenue marketers/advertisers by whom to promote simplistic notion facial idea that they moisturizing the skin. The heavenly desire to being applying as such oily materials under skin is almost impulsive, and it can be the dawn of older time itself. From that time the materials which are used to promoting appearances or to beautify the skin are also known to be considered as cosmetics [6].

Traditionally, moisturizers are being once likely to preventing TEWL (Transepidermal water loss) by occlusion (but now in combination only), prevent dryness, even adding to skin smoothens with elastic maintenance. SC (Stratum Corneum) although the deadly layer which acts as an active membrane as suggested by bricks and mortar model [13]. Corneocytes are the bricks having their tough cell membranes with keratin microfibrils, while lipids layers between the cells present are the mortar. The predominant loss of intercellular lipids, i.e., by skin humidity regulation due to the forming of bilayers such as ceramides, cholesterol & fatty acids which resulting bilayers damaging water barrier formation which leads to dry skin. When this moisture content of the skin falls below 10%, then the SC losses its continuity which considered as dry skin (as shown in **Figure 2**) [6,9].

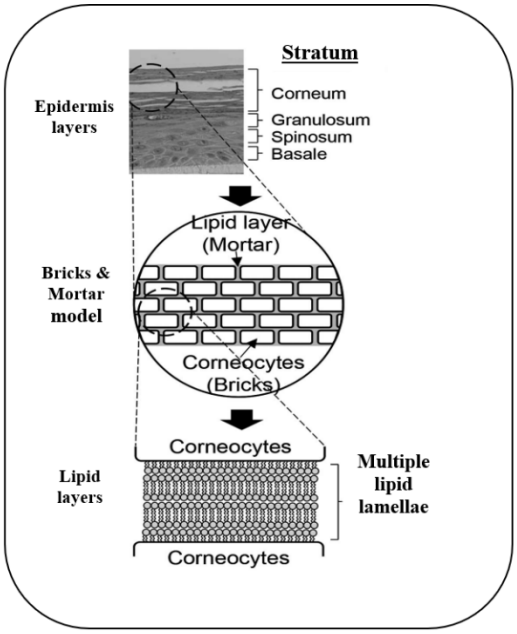

Figure 2. Structure of multiple lamellae in which the SC formed under corneocytes (bricks) & lipids (mortar). Intercellular voids surround with many intercellular lamelle are abundant in the packed lipid layer. Where it depends on the ceramide kinds, the lamellar organization is categorized as either LPP (Long Periodicity Phase) & SPP (Short Periodicity Phase) [12].

3. Ideal properties of moisturizer cream

An ideal moisturizer is a difficult task due to their needs and results which are highly personalized. However, it must have some attributes that makes them suitable under various conditions with their applications [6]:

1) It should reduce and prevent further TEWL.
2) It should restore by duplicating and enhancing the skin's moisturizing retention process lipid barrier in order to reestablishing the lipid barrier.
3) It should able to leave the skin feeling soft rather than sticky.
4) It should hypoallergic, non-sensitizing, fragrance free and non-comedogenic.
5) It should be absorbed immediately, providing immediate hydration.
6) It should reduce dryness and improve dull appearance of skin.
7) It should cosmetically acceptable.

4. Anatomy and physiology of skin

Skin is the largest and the most readily accessible and have largest organ of the human body in term of surface area and body weight in which having surface area of approximately 1.5–2 m^2 and skin represent 8% of body weight in adults. The structure and its functions of skin also known as the integumentary system. It is the outermost layer or tissue of the living body. In certain areas, it contains accessory structures: glands, hairs & nails. Skin shows a protective mechanism from external environment. Skin can produce a favorable chemical substance named as Vitamin D when skin exposed to sunlight. The skin helps to regulate the temperature of human body and also acts as sensory organ. Skin includes various cellular elements like melanocytes,

erythrocytes, keratinocytes, Langerhan's cells & Merkel's cells having multi-layer structures because of different components like cells and fibers (as shown in **Figure 3)** [14,15].

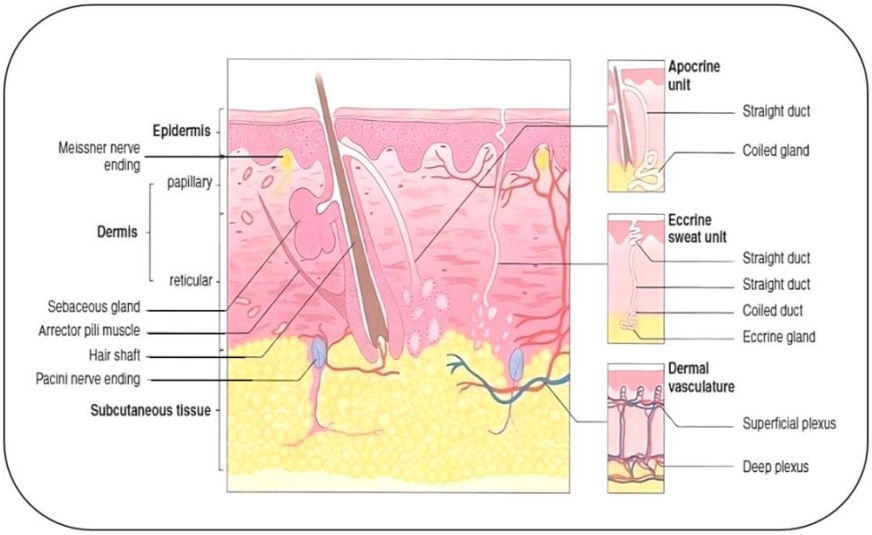

Figure 3. The cross-sectional view of human skin consists of three different layers as epidermis, dermis and subcutaneous tissues [15].

The skin consists of three skin layers:

4.1. Epidermis

It is the outer part layer of skin known as epidermis having thickness of about 0.2 mm. It is the most superficial layer and is composed of stratified keratinsedsquamous epithelium. There as such no blood vessels or the nerve endings are located under this layer, but in deeper layers, they are bathed with interstitial fluid from the dermis providing the oxygen & nutrients which are drained apart lymph. But, the thickness of epidermis is primarily composed depending upon mainly two cells types that are keratinocytes and dendrites cells. The epidermis layer is also called as the metabolic active tissue [14]. The epidermis is a continually renewing layer which gives rise to derivative structures under pilosebaceous apparatuses, nails and sweat glands where its basal cells stats poliferation providing renewal of the outer surface. The epidermis is basically dynamic tissue that constantly unsynchronized motion, as differ as individual cell populations [16]. But its keratinocytes bit differs from the "clear" dendritic cells by possess intercellular bridges and ample amounts of stainable cytoplasm. In this, the last three layers constitute living, nucleated cells referred to as stratum malpighii and rete malpighii. The epidermis protects others populations of cells such as melanoctyes, Langerhans cells and Merkel cells. But, as in keratinocyte cell type comprises of majority of cells far [17].

The epidermis outermost layer is made up of five sub-layers based on the keratinocyte morphological positioning as differentiation follows (as shown in **Figure 4**):

1) Stratum corneum (~Commonly known as Cornified/Horny cell layer)
2) Stratum lucidium (~Commonly known as Clear cell layer)

3) Stratum granulosum (~Commonly known as Granular cell layer)
4) Stratum spinosum (~Commonly known as Squamous/Pickle cell layer)
5) Stratum germinativum/basale (~Commonly known as Germinating/Basal cell layer)

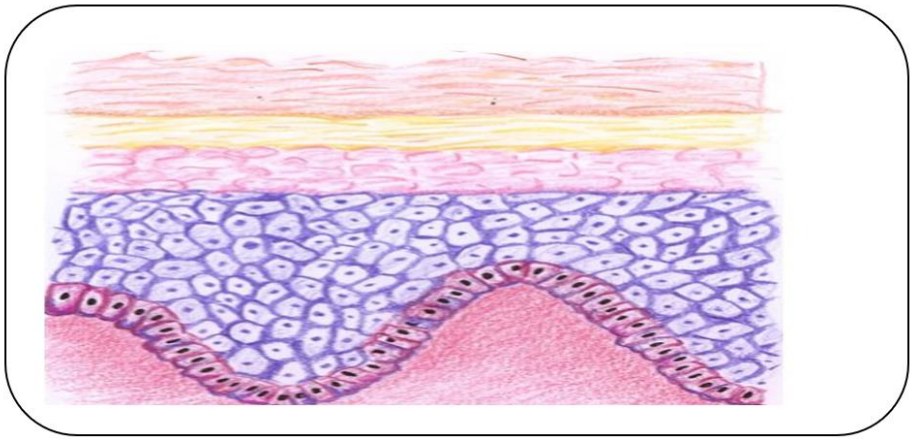

Figure 4. Diagrammatic cross-section of epidermis in detail layers of the human skin [16].

4.1.1. Stratum corneum (SC) [16,18]

The exterior sublayer of the epidermis which is also referred as the horny cell layer having thickness of about 8–15 μm.

- It provides mechanical protection to the underlying epidermis and as preventive water loss barrier and invasion by foreign substances.
- This layer is of hexagonal shaped like scaly cells like which are constantly shed (corn flakes) is helpful for prevention of skin from the large amount of dehydration.
- They are rich in protein and low lipid content surrounded by continuous extracellular lipid matrix.
- It also contains “ceramide” which is main component having role in water retention.
- The cells are large, flat, polyhedral-shaped horny cells have loose nuclei during terminal differentiation, technically considered as dead cells.
- The physical and biochemical cells properties vary depending upon position to order desquamation moving forward upward.
- The deep cells are also more densely compact and display a greater array of intercellular attachments than the more superficial layers.
- The entire layer is being replaced during period of about 4 weeks during cosmetic procedures such as microdermabrasion, help to remove dry, upper layer aiming to get looking “fresh” and healthy skin.

4.1.2. Stratum lucidium [16–18]

- It is composed of as smooth, thin clear or transparent cell layer of dead skin in which light can pass.

- It is only area that found only in thick skin on the hand's palms, soles and digits of feet.
- The keratinocytes in this layer composed of dead and flattened.
- These cells are densely packed with eleiden, a clear protein rich in lipids derived from keratohyaline granules gives the cells transparent appearance and provides barrier to water

4.1.3. Stratum granulosum [16,19]

- It is most superficial layer containing living cells also referred as granular cell layer having thickness 1–3 μm containing 2–4 layers lying proportion to thickness overlying SC.
- The shape of the flattened cells is flatter holding distinct due to the keratin fibers are increasingly produced & filled up into the cells in their cytoplasm.
- These cells responsible for further synthesis and modification of proteins involved in keratinization.
- A very thin or absent granular layer can lead to extensive parakeratinosis in which the keratinocyte nuclei persist as the cells move into SC, resulting psoriasis.
- The enzymatic action of keratohyaline granules necessary for holding keratin filaments together and inner lining of SC results in production of "soft" keratin in epidermis providing periodic cutting of keratin filaments. Where, the tonofibril filaments traversing cell cytoplasm harden due to incorporation of disulfide bonds, producing hard keratin structures.
- Exception of hair and nails, they not possess keratohyaline granules.

4.1.4. Stratum spinosum [16,19]

- It is also referred to as squamous or pickle cell layer having thickness range 50–150 μm containing 3–6 layers thick.
- It consists of number of cells, which may differ in shape, structure and even dividing constantly depending on their location.
- Although, the lamellar granules are active cells at the interface between the granular and cornified cells as they also function in cells of upper spinous layer to deliver SC lipids into the intercellular spaces.
- Intercellular spaces between spinous cells bridged abundant desmosomes that promote mechanical coupling between epidermis cells resistant to physical stress.
- Gap junctions are another type between epidermal cells forming an intercellular pore, allowing physiologic chemical signals transmit that is vital in the regulation of cell metabolism, growth and differentiation.

4.1.5. Stratum basale [16–18]

- It is also referred as basal/germinating cell layer which composed as single layer and is the deepest & sublayer of epidermis.
- In this, keratinocytes are produced and shows their movement upward to the outer surface that attach to basement membrane zone with their long axis perpendicular to dermis. This movement of keratinocytes referred as "turnover".

- These basal cells are forming a single layer adhering to one another through dermatosomal junctions as they are dark staining oval and elongated nuclei which are mitotically active cells.
- The epidermis cells produced under this layer in which to complete one cycle of this process takes days & keratinocytes also change their function and structure slowly under normal conditions.
- It holds 8% of water in epidermis.
- Each distant nuclei contained by epidermis cells are continuously divided under process refer as mitosis.
- It also home of *melanocytes* that producing the pigment called melanin (skin colour responsible) while exposing to sunlight produce better production of more melanin to better skin protection from UV exposure.
- Migration of a basal cell from the basal layer to the SC in humans takes at least 14 days and to get tramsmit to the outermost epidermis require another 14 days.

4.2. Dermis

This layer is mainly referred to as the true skin which forming bulk of the skin containing good blood vessels & lymph supply providing by the lymph capillaries, arterioles and veinules that nourishing the skin & eliminates waste products or toxins. This layer is an integrated system of fibrous, filamentous and amorphous connective that accommodates stimulus-induced entry by nerve and vascular networks, epidermally derived appendages, fibroblasts, macrophages and mast cells. It protects the body from mechanical injury, binds water, aids in thermal regulation and includes receptors of sensory stimuli. Sweat glands are present in this region that creates sweat through pores, removing impurities as cool body. The hair follicles & sebaceous glands, which produce the oils which make the skin soft & smooth the skin sometimes "over-zealously resulting in rashes and in oily skin are also found in dermis". Most of the magic happens in the dermis region at least in skin [14].

The dermis interacts with the epidermis to maintain the properties of both tissues were the two regions collaborate during development in the morphogenesis of the dermal-epidermal junction and epidernal appendages interact in repairing and remodeling the skin as wounds are healed [15]. Even, the dermis is made up of two layers of connective tissue that compose an interconnected mesh of elastin and collagenous fibers, produced by fibroblasts [15,16].

Those layers of connective tissues consisting into two stained slide components:

4.2.1. Papillary layer [16]

- It directly situated under epidermis which quite thin and have cone like projections called papillae extending into epdermis.
- It is made of loose, areolar connective tissue which means the collagen and elastin fibers form a loose mesh.
- It providing nutrients & oxygen under basal layer of the epidermis.
- This superficial layer of dermis projects into stratum basale of epidermis to form finger-like dermal papillae.
- Within the papillary layer are fibroblasts, a small number of fat cells (adipocytes), and an abundance of small blood vessels.

- It also contains phagocytes, defensive mechanism that helps to fright bacteria or other infections that have breached the skin
- This layer also contains lymphatic capillaries, nerve fibers and touch receptors called the Meissner corpuscles.

4.2.2. Reticular layer [16–18]

- It situated below the papillary layer where the main dermis consists of collagen and elastic fibers.
- Underlying papillary, it is much thicker and composed of dense, irregular connective tissue represents 70% of dry skin's weight.
- This layer is well vascularized, appear recticulated (net-like) due to tight meshwork of fibers and have a rich sensory and sympathetic nerve supply.
- Collagen fibers provide structure and tensile strength, with strands of collagen extending into both the papillary and the hypodermis. It even binds with water to keep skin hydrated.
- Collagen is a major stress-resistant material of skin and even exists in a constant state of flux, being degraded by proteolytic enzymes called spare collagenases which replaced by new fibers.
- Collagen gives the skin a plump and youthful appearance which is white fibrous tissue made up of proteins.
- Elastin fibers provide skin elasticity nature made up of yellow elastic tissue. The fibers produced by the fibroblasts in which all are held together in a ground substance enable movement.
- The network is strong where skin remains youthful and firm. However, fibers hardening and splitting the network collapses and ageing process starts which get become naked.
- The fibroblasts fuse with elastic fiber to the extracellular matrix of the dermis which is composed of glycosaminoglycans.

4.3. The subcutaneous layer (hypodermis or superficial fascia)

The deepest layer of skin is the sheet fat-containing areolar tissues known as the superficial fascia that connects bones to muscles and deep that the active ingredients in skincare products never reach. This layer is like a thermostat which protects, insulate, cushions and supports the body. It is not strictly a part of skin, although the border between the hypodermis and dermis being difficult to distinguish. The lobules of fat cells are separated by fibrous septa made up of large blood vessels and collagen. It generally made up of fat cells (adipose tissues/lipocytes) acts as a filter, protecting muscles, bones & organs from damage. The amount of fat under face is beneficial contours making the face look more youthful. It also contains additional blood vessels, nerve endings, hair follicular roots & the deepest oil-producing sebaceous glands [14]. Another location under processing and regulation of androgen is the sebaceous gland. The skin even contains all the enzymes needed for converting cholesterol to steroid precursor or adrenal hormones. As an exocrine gland, the hypodermis tissue provides the body with buoyancy and functions as storehouse of energy in a pinch [16].

5. Morphological skin diseases treat using moisturizer cream

The scaling and roughness are the naked features of dry skin for clinically aid patients. Thus, the accumulation of scale on skin surface results of enhanced production of comeocytesor delayed desequamation. Closer examination of the dry skin surface by scanning electron microscope (SEM) showing coarser, broad, irregularily running furrows and loss of minor furrows compared to normal skin [11].

The SC even more soft and compliant to their mechanical stimuli when hydrated where water have plasticizing effect which allowing the layers to bend and stretch more easily. Thus, avoiding cracking and fissuring. The water content must be more than 10% for the skin shows the normal appearance and function [17]. An active site of lipid synthesis under epidermis are being largely unaffected from the influence of circulating lipids. Where, phospholipids and glycosphingolipids which get hydrolyzed into ceramides and free fatty acids (as shown in **Figure 5**) [18].

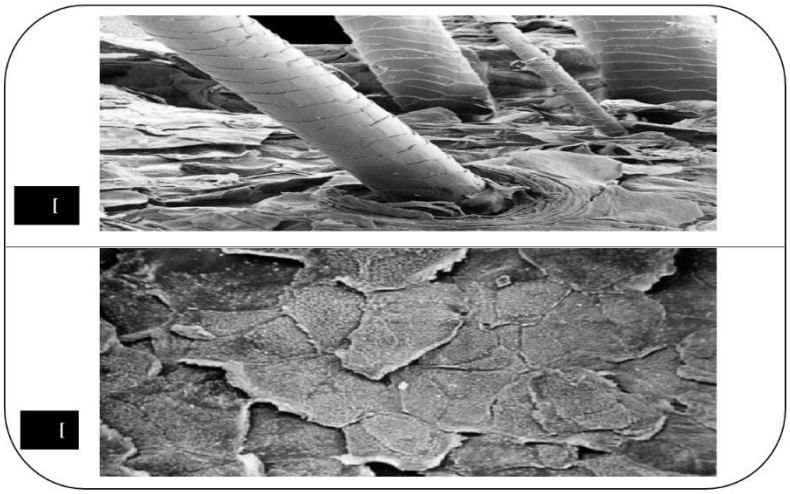

Figure 5. As in upper part show SEM view of human skin containing hair shafts growing through it where as in lower part show SEM view of common dry skin [15].

This review being emphasizes the use of moisturizers in various dermatitis treatment such as atopic, seborrheic, contact and nummular dermatitis as follows along with treatment specifications of specific treatment needs:

5.1. Atopic dermatitis with its skin treatment

It is basically a chronic skin inflammation being characterized with pruritus and skin barrier effect. The skin structural protein and filaggerin is genetically mutated leads to malfunction skin barrier causing severe disorder development. These mutations being hamper expression of filaggerin which is structural protein responsible for maintain integral barrier of epidermis as skin's vital defense line. Due to filaggerin deficiency, skin barrier deficiency causes enhanced TEWL, facilitating exposures of environmental allergens and infective organisms through skin leading persistant skin inflammation [20]. Due to its relapsing nature, its treatment and prevention management of flares requiring long-term barrier restoration of skin providing patient counseling and caregiver's partnership [21].

Moisturizers are important in this for the optimal recovery of disorder regardless the severity which can penetrate and help to recognize skin layers structure. So, they recommended as a key step for treatment with triggers avoidance and measures to control inflammation [21]. The choice of disease treatment use of ingredients that carefully sees the patients are more prone to contact dermatitis as in population. Some of their treatment of them are as follows [22]:

1) Natural oils being widely used as ingredient for prevention but there as such few data as available regarding safety and efficiency profile. Suggesting low oleic acid and high linoleic acid ratio in natural oils determines hydrating and protecting effects on skin being shows positive effects. Safflower oil, sunflower seed oil and sea buckthorn seed oil have high oleic acid and linoleic acid ratios. But, olive oil has low oleic acid and linoleic acid ratios which can destroy skin barrier by disruption of SC. But still, they all need in dermatoses treatment.
2) Humectants such as urea (10%) shown to reducing TEWL in this treatment. But it an also reduce exposure of sodium lauryl sulfate causing skin irritaion in both diseased and normal skin. Alphahydroxy acids are also effective treatmentsfor dry skin. As, (L isomer)-lactic acid stimulates ceramides synthesis causing SC production and promoting dry skin and its lipid barrier resistance.
3) Emollients or humectants being incorporated with anti-inflammatory agents providesbarrier repairing and dry skin which are being carefully selected for particular patients.
4) Ceramides restore skin water permeability and barrier function of diseased skin in which 50% high ceramide composition of skin naturally possessed by SC. The tropical mixtures of SC lipids consisting of ceramide, cholesterol and free fatty acids known as physiologic (3:3:1 proportions) accelerates barrier repairment. Unlike non-physiologic lipid such as petrolatum traverse both intact and disrupted SC. Nanoencapsulatedtriceramides being used asimprove skin hydration.
5) Niacinamides improving skin barrier functions enhance epidermal ceramide and other intercellular lipid levels. It decreases TEWL in atopic dry skin significant better compared to white petrolactum. It results more rapid and sustained skin dryness and improve SC barrier.
6) Aloe vera, Bisabolol (extracted from *Matricaria recutita* plant), Shea butter (fat derivation of *Butyrospermumparkii* kernals) and Glycyrrhetinic acid (extracted from *Glycyrrhizainflata* root) are all herbals effective treatment for various inflammations, tumors, pruritus, wound burn acceleration and many more significant benefits even also for scalp inflammatory patients. While, Zinc gluconate being only effective in treatment of anti-inflammatory may target to poliferator-activated receptors-α (PPARs-α), human beta-defensin-2 and psoriasin.
7) Palmitoylethanolamide an endogenous lipid from fatty acid resembling SC components and functions possess both anti-inflammatory and analgesic properties treat mild to moderate severe patients used via by moisturizer being useful to improve pruruitus, dryness and eczema lesions.

5.2. Seborrheic dermatitis with its skin treatment

It is a chronic-recurrent skin inflammation disorder mainly affects the male adult patients causing in duration puberty due to cutaneous lipids abundance from increasing androgen-driven sweat gland development and sebum secretion. It commonly affects at scalp, face and periauricular region, even also at central chest, axillae and genital region. Pruritus and lesions are rarely caused. Epidermal barrier integrity, host immune response, neurogenic factors, emotional stress and nutritional factors are some susceptible. In this, alterations of corneodesmosomal hydrolysis and impared lipid organization were observed causing desquamation disruption include corneocyte shape and epidermal barrier structural abnormalities in scalp dandruff. Therefore, histamine and oleic acid being prone with the high itch perception or flakes [23,24].

The associated symptoms based on disorder severity and relapse tendency of this therapy available treatment for alleviate visible signs options includes [22]:

1) Nonsteroidal tropical device cream is water based fragnance free cream as medical device to manage and relive this disorder such as itching, erythema, scaling and pain. The ingredients being contributes to system improvement are Biocide piroctone olamine, many antioxidants (such as Telmesteine, Tocopheryl acetate, Ascorbyltetraiso-palmitate), many skins conditioning agents (such as Ethylhexylpalmitate, Bisabolol, Shea butter and *Vitisvinifera*) and Alglycera (composed of Allantoin and Glycyrrhetinic acid). This cream is evaluated use for anti-fungal effect which being effective for this disorder. Even further timing of this disorder relapse rate with different therapeutic agents.
2) Ketoconazole (2%), Cyclopirox (1%) and Pimecrolimus (1%) creams for treating mild to moderate disorder. Except Pimecrolimus (1%) cream for using longer period to prevent relapse without adverse effects concerned. A short course of tropical corticosteroids on potency with combine nonsteroidal agent is rational therapeutic choice.

5.3. Contact dermatitis with itsskin treatment

It is a common skin inflammation disorder being characterized by pruritic and erythematous skin lesions inducing via contact with foreign substances as divided into two causative groups are irritant and allergic, along with skin's affected area mainly depends. It appears as erythema, vesicles, bullae and scaling with relatively well-demarcated and visible borders. It affects on hands, neck and face or in any other area of skin. Patients being complaining of itching and discomfort, but some seek medical care appearance of rashes. In chronic case, lichen with cracks and fissures. Patient history might crucial and being resolved to avoid this disorder to prevent over enhancement. However, difference between irritant and allergic in clinically impossible. So, these agents are successful for irritant contact dermatitis. Thus, there as such insufficient data for tropical corticosteroids in irritant contact dermatitis [25,26].

Patients suffered from this disorder must take primary precautions such as personal protective equipments are gloves, googles, face shields and other protective equipments in which cotton liners under gloves shows comfort and swat absorption

[26]. Even make the skin clean, dry and moisturized as well. Some other secondary measures also take place to prevent the disorder as follows [22]:

1) The patients must wash their skin with lukewarm water and use mild soaps and then gently dried. After that soap must be removed careful at spaces of fringer web due to surface active agents provides alkaline nature cause non-gentle for skin. Some metal accessory such as gold rings might harm to moisten and trap those allergens.
2) Emollients are good preventors as after work of cream as for workers use them regularly. Barrier creams (specialized creams) often provide barrier creams containing quaternium-18 bentonite (organoclay) prevents rhus dermatitis or creams chelators content as penta-acetic acid helps to provide protection from nickel, chrome and copper dermatitis. Cochrane as barrier creams as short-term protective effects and also non-promoting effective prevention for workers.
3) Lipid based moisturizers are also routinely used to strengthens skin barrier function. While overnight application of proper emollients being recommended.
4) Oilments also suggested over creams helpful for sensitizing preservatives and midly irritating emulsifiers. Petroleum based emollients containing lipids and tropical mixtures of key SC includes ceramides to accelerate barrier repairment. The soak and smear method been applied for mid to severe potency tropical corticosteroid oilments or emollients over damed skin mean “lock in moisturizer”.
5) Canola oil derived sterol-enriched fraction shows ameilorate which is sodium lauryl sulfate-inducer mean irritant preventor and supplies the damaged skin with adequate lipid for healing whereas Fish oil, Petrolactum, Shea butter, Sunflower seed oil and other lipids had no effect on irritation. Even essential fatty acids such as Linoleic acid and Alpha- linoleic acid influence skin barrier functions such as eicosanoids production, fluid membrane and cell signaling.
6) Squalene is the sebum component that a single oxygen quencher protecting the skin from lipid peroxidation from UV and other irritation exposure. It is saturated form hydrogenated elimination of double bonds making oxidation resistant and as good moisturizers. As in technical oil form which is less grasy, odourless, non-comedogenic, anti-bacertial and sensitivity safe nature. Even helpful for other skin disorders treatments as atopic and seborrheic dermatitis.

5.4. Nummular dermatitis with its skin treatment

It is also known as nummular eczema an eczematous disorder causing prurtic coin—shaped patches on the skin that are often mistake for ringworms or psoriasis. Mostly women usually get affected sooner than men. But most of patients suffered from dry skin causing epidermal breach and allergens permeation. Patients being complain about burning or stinging eruption on leys within days or months. Sometimes, nickel, cobalt or chromates might cause of this disorder. Local trauma includes chemical contact, arthopod bites and abrasions may outbreak. Symptoms of wax and wane winter, cold or dry climates are been exacerbated by temperature swings and been improve with sunlight, humidity exposure or moisturizer use. But it cannot be cause on face and scalp regions. In severe case, may being associated with Interferon and Ribavirin therapy for hepatitis C and tumor necrosis inhibitors [27,28].

Diagnosis is made being observed and treatments aimed at skin rehydration, epidermal lipid barrier repairment and infection control, even cleansing modifications recommended. Also, for primary measures, gloves and protected tools affected in use for hands ensure skin avoided from solvents, detergents, friction other chemicals or excessive exposures [28]. So, the secondary measures are taken for the disorder treatment as follows [22]:

1) Soaps are applied at axilla and groin redions whereas soapless, lukewarm and cool showers applying moisturizers or medicated tropical application on damp skin may alleviate itching and skin rehydration resulting effective penetration and faster heal.
2) Wet rap treatment effective involving skin dampening or tropical oilment corticosteroids whereas plastic wrap can be used for occlusion of small areas. It been carefully monitored for avoiding adverse effect over usage. In this, oilments are effective than creams due to excessive skin barrier occlusion under environment.
3) Emollients consisting of bath oils, soap and moisturizing creams as prevention from itching, scaling and dryness and being unaffected skin to overcome dryness. Some effective emollients are Sorbolene, Glycerine and Cetomacrogol creams, Whit soft paraffin or Liquid paraffin mixture, Fatty cream and Wool fat lotions. Even heavy moisturizers or petrolactum applied to damped skin often effective use only 5–6 times a day.

6. Functions of skin

They consist of various functions of skin includes:

6.1. Sensation

It consisting range of nerve endings which respond or acts sense organ for detecting changes in the environment such as cold, heat, pressure, touch, vibration, tissue injury and even pain [29]. Skin represents as ‘sense-of-touch’ that triggers a response if we touch or feel something to patients with skin conditions in which extreme itching and great distress. Also touch being important for patients who feel isolated by skin resulting colour, disorders or perceptions of others as experiencing dirt or contagious foreign substances [30].

6.2. Heat regulation/thermoregulation

Skin’s one of important function is body protection from heat or cold temperatures. The skin blood supply is more than its needs which allowing fine control of energy loss by conduction, convection and radiation where alterations of blood flow through the cutaneous vascular bed [14,30]. Even helps the body at contact temperature of 37℃ with variation between 0.5℃ to 0.75℃ by dilating to promote perfusion as well as heat loss while constriction significantly restrict cutaneous of blood vessels and maintains body heat. Evaporation and secretion of sweat glands keeps body cool whereas subcutaneous adipose tissues insulating the body. It can also be achieved by sweating produced by eccrine sweat glands [30,31].

6.3. Absorption

Skin mainly absorbs substances from outside the body through the process called absorption or percutaneous absorption. The skin has limited absorption capacity, but it can absorb certain particles that small enough to get absorb such as ingredients within facial creams, hormones, etc. which affect the person exposed to being affected by chemicals or agents so that proper medication takes place [30]. Skin provides a physical barrier against the external environment and helps to reduce water loss by means of water-impermeable SC. Even the drugs those with low molecular weight can passes under barrier of skin [31].

6.4. Body protection

A water-repellent anatomical barrier which protecting the body against bacterial infection, dehydration, dirt and chemical attack between external & internal environment in bodily defense by which the acid mantle pH 5.5 (from sebum & sweat) discouraging bacteria and fungi growth whereas melanin under epidermis protecting against damages caused by UV rays. Even defense the skin as a barrier from mechanical, thermal, injury, moisture loss and proteins [14,32].

6.5. Storage and synthesis

By UV rays action on specific areas of skin which serves as storage site for lipids, proteins and water content. Sun's UV rays even help in natural vitamin D production and also helpful to manufacture melanin pigment. The process in skin such as formation of melanin, vascularity and keratinization help to determine the coat color and skin. In which pigmentation of skin helps to prevent damage from solar radiation [31].

6.6. Water resistance

The skin performs as water resistant barrier preventing body's vital nutrients from being rinsed away. Thus, essential nutrients are not washed out of the body. Therefore, the outermost layer skin epidermis consists of the dead cells which serve as the major water proof action for the skin. As the skin allow smooth movement of the body [33,34].

6.7. Excretion

Waste products including lactic acid, urea (from kidneys) and salts such as sodium chloride (from sweat) are all lost via perspiration. Also, it is one of the major ways of the body homeostasis which the skin under circulation. As sweat glands automatically mature, therefore its small fraction of these glands are functionally mature with secretory function [17,31].

6.8. Immunity with secretion

The skin is an important immunological organ, made up of key structures and cells that helps and fight against pathogens [16]. Skin secretes products from sebum, sweat and pheromones and exerts important immunological functions by secreting bioactive substances such as cytokines (chemical messenger) involved which makes

the cell and their function specialized. Sebum which gets secreted by the sebaceous glands maintain skin hydration and nourish [31].

6.9. Controlling evaporation

The skin as a semi-permeable that relatively dried against fluid loss, due to significant fluid loss in burns resulting loss of function. Thus, the TEWL describes the content of water loss through epidermis through evaporation [31]. Skin evaporation also depends on various factors includes blood flow, local haemodyamics, corneocyte degree formation and SC lipid content. Even there is a direct link between TEWL and skin development mean lower skin impedance indicates higher skin hydration as functional barrier to evaporating water loss [32].

6.10. Biochemical production

Actually, the skin involved in several biochemical processes. This occurs when the sunlight rays on the skin producing this chemical reaction derived from 7-dehydrocholesterol under fatty substances [30]. Where, vitamin D is the essential of Calcium and Phosphorous absorption required for healthy bones. Even, the skin also contains receptors of other steroidal hormones such as oestrogens, progestrogens and glucocorticoids and for vitamin A [33].

6.11. Aesthetics and communication

Others can see and judgment our emotions, physical conditions & beauty based appearances of skin. This appearance in a way such a glossy to feel having aid of beneficial effects making the skin smooth, fluffy and moisten the skin via makes good looks making the person judgmental of skin. For example, a person having skin color or skin presence is fearful or disordered, the other person visible its beauty and imageful thought as per society might be the way of patients are accepted as important consideration of medicated experts [31,34].

7. Tropical drug delivery of moisturizers cream

Over decades, the illness treatment is being fulfilling by administering drugs to human body via various routes namely oral, sublingual, rectal, parental, inhalation, etc. Tropical delivery be defined as the drug application containing formulations to the skin directly treat cutaneous disorder or its manifestations of general diseases intending the therapeutic effect of drug at the surface of skin semisolid formulations in all their pharmaceutical system for tropical delivery [20]. The challenge of tropical drug delivery is being transport across the SC [35].

Tropical vehicles are used as carrier systems which aid with active drugs across the SC to deep regional layers while minimizing absorption into the systemic circulation. However tropical moisturizing creams as cosmetics used as emollient therapy use to ameliorate dry skin conditions such as eczema and psoriasis where moisturizers use become pivotal as first-line treatment strategies. Tropical vehicles act as chose based upon the nature such as in wet, dry, mucous, non-mucous, healthy and diseased climatic skin conditions. As well as, the size of skin area is being treated to optimize applications on skin contact with the products [36].

Delivery of such drug molecules of skin involves the complex intermediate between the active drug, tropical carrier system type or vehicle with excipients choice. The tropical carrier system or vehicle refers to the substance that carries the chosen active drug into contact with and through the skin at an appropriate level to provide therapeutic effect [37]. Even it contains synergistic blend of moisturizing agents which help to improve efficacy and it must be cosmetically accepted in need to balance the heaviness of a moisturizer is one that the patient willing to use [36,38]. Dry skin as being unable to efficiently bind and hold water and favors the penetration of irritants, allergens and microorganisms providing discomfort and itchiness, as well as visible irritation or redness and also need to protect both health and dry skin conditions for preserve and restore its functional and structural integrity [38].

The intact of SC (as shown in **Figure 6**) is considered as the major barrier of penetration of drug, as it impermeable to almost all compounds and molecules under the molecular weight must be more than 600 Daltons [39]. Diffusion along with the concentration gradient is the principle mechanism of drug across the skin permeation takes place [40]. Generally, there are two pathways or routes to penetrate the SC as the trans epidermal route and the trans appendageal route as shown in **Figure 7**.

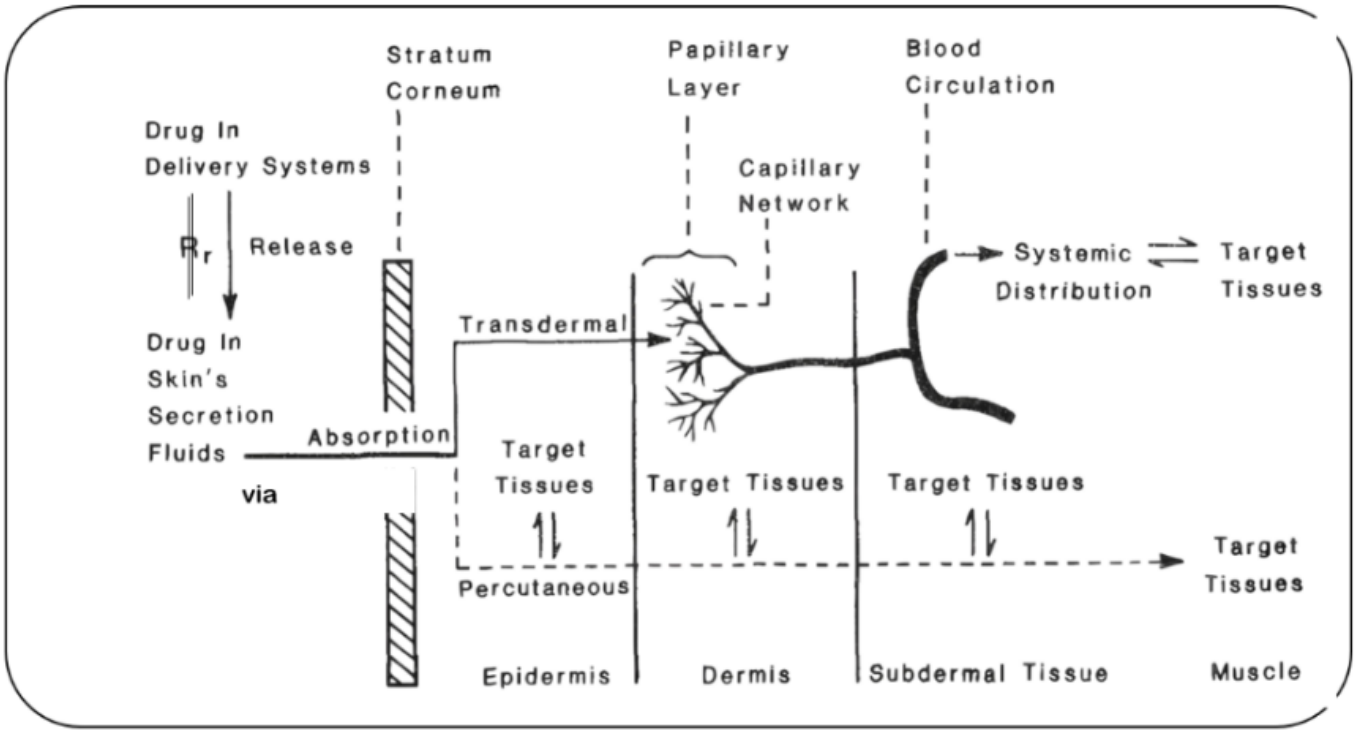

Figure 6. The skin tissues absorption across for localized therapeutic action in tissue directly underneath the site of drug administration to the systemic medication where the transdermal permeation of drug underneath uptake by the capillary network in the dermoepidermal junction takes for systemic distribution takes place [35].

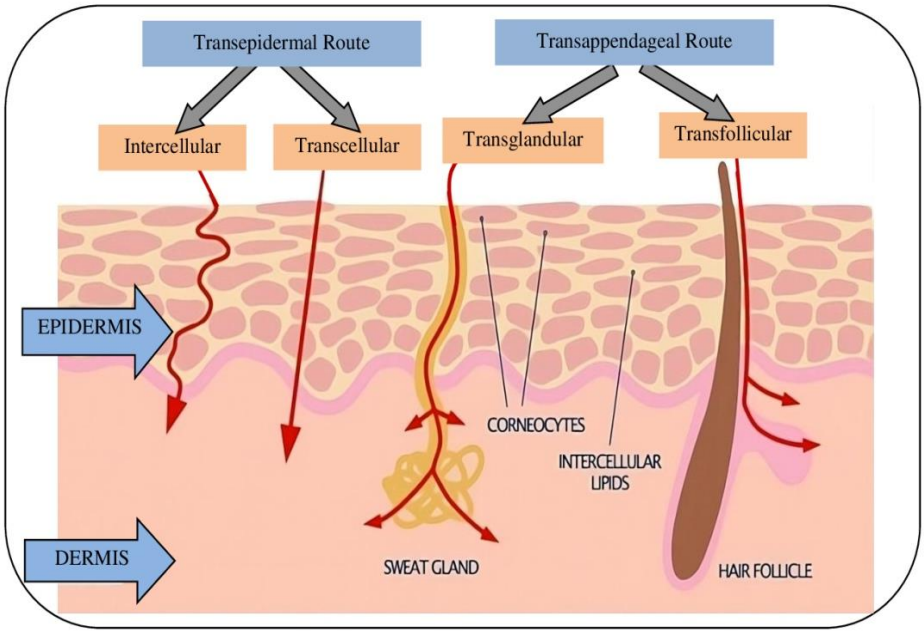

Figure 7. The penetration pathways/routes of the skin epidermis layer [40].

7.1. Trans epidermal pathway

This pathway consists of two micropathways are intercellular and trancellular route. In this, the most common pathway of permeate the skin is the intercellular pathway in which the drug content diffusing around the corneocytes and the continuous matrix. The interdigitating nature of corneocytes yields the curved pathway which in contrast relative to the way of transcellular pathway. Whereas, the transellular route is the most direct path for the cream's vehicles containing drugs to permeate the skin. It requires the drug to transverse the alternating layers of corneocytes and extracellular matrix involves a sequence of partitioning and diffusion into alternating hydrophillic and lipophillic domains [40]. Small hydrophillic molecules generally favor the transcellular route over the intercellular pathway vice versa for lipophilic molecules. The estimation value 50 times of water travel to intercellular pathway than the thickness of the SC [36].

7.2. Transsppendageal/shunt route pathway

This involves the flow of drug molecules through the sweat glands and hair follicules which can be vital for ions and large polar molecules due to not freely cross the SC. This pathway provides a continuous channel directly across the SC barrier. It is generally required due to the surface area being surrounded by sweat glands and hair follicles being small, typically 0.1% of skin's total surface area and their epidermal contributed permeation usually small [41]. But due to large polar molecules or ions, it cannot be freely cross the SC [36]. Therefore, sweat glands provide a hydrophillic pathway across the skin due to the secretion of aqueous salt solution, permeation being limited as sweat moves to reverse direction of that drug. Thus, sebaceous glands are filled with a lipid-rich sebum, being presenting a barrier to hydrophilic drugs [42].

8. General mechanism of action of moisurizing cream

The basic principle of moisturizers is to improve skin moisture intended to supplement barrier lipid deficiency and improves skin barrier function. So, the basic moisturizers with a good combination of hydrophillic and lipophillic ingredients being formed products lower fragnance and allergens being recommend. The lower lipid content of SC will better the penetration local fat-rich agents, better the dries basis. More lipids containing moisturizers content base can quickly relieve drysympotoms via suppressing loss of moisture [43].

The skin function serves as the barrier protecting the tissues from the desiccation, mechanical stress, infection, and chemical irritation of underlying tissues Enhancement of TEWL associated with various kinds of dermatitis leads to impaired function [44]. After moving upward to hydrate SC cells, water from deeper epidermal layers and then lost to evaporation. Epidermal water content and plasticity maintenance is essential to prevent skin dryness. SC is an active membrane, described previously under bricks and mortar model, where loss of intercellular lipids, forming the bilayers (include ceramides, cholesterol & fatty acids) which leads to water barrier formation damage leads to dry skin. The pivotal factor structure of the SC under skin is water flux, retention and overall moisturizing level [45].

There are four key processes in SC formation and functioning as shown in **Figure 8.** Where SC formation and functioning patterns showing in the skin epidermis where moisurizing effect is naturally depends.

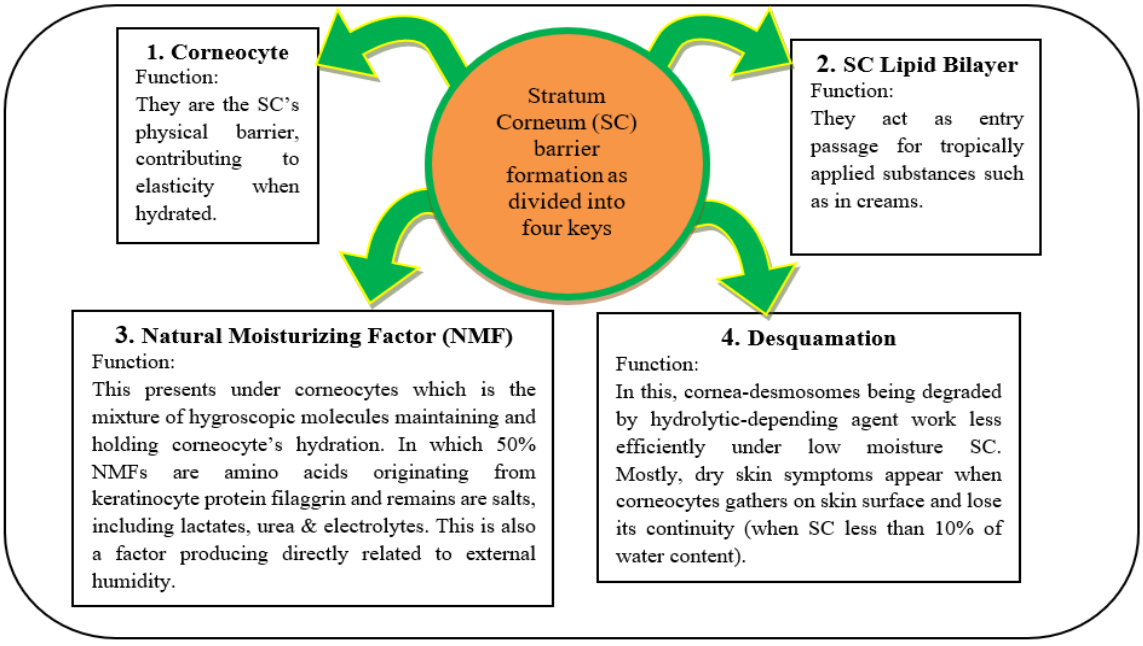

Figure 8. The four key processes under SC formation and functions which involves the natural moisturizers effects process under the skin surface [46].

Moisturizers improve skin barrier repair, maintain skin's integrity and appearance by acting as humectants, emollients and occlusives based on their own action mechanism. By directly providing water to the skin from their water phase and

increasing occlusion to reduce trans-epidermal water loss, moisurizers improve the skin barrier repair function, maintain skin's integrity, appearance, improves skin hydration. They improve SC water content and also covers small skin fissures providing soothing protective film and protecting skin from friction [9].

Additionally, moisturizers application even smooths skin surface by filling via spaces between restoring intercellular lipid bilayers to absorb, retain and redistribute water partially and desquamated skin flakes. Mechanism of skin changes accumulately enhanced hydration facilitating breakdown of corneodesmosomes and preventing corneocytes building up and even promoting its continuity. According to Loden statements, skincare products only penetrate to influence the skin's structure and function, in addition, it also stays inactively on the skin surface [47].

Moisturizers are also helpful in smoothening effects by having the phenolic compounds on inflammation. Free radical (ion superoxide) scavenging will occur introduce to hydroy radicals (OH-) and to their double bonds. In the same way heavy metal ions will be trapped, which are present in polluted air and particularly attack sensitive or allergic skin condition [48]. The appearance and function of creams via at skin surface maintains the important balance of water content between skin surface lipids represents superficial layer of the body (as shown in **Figure 9**).

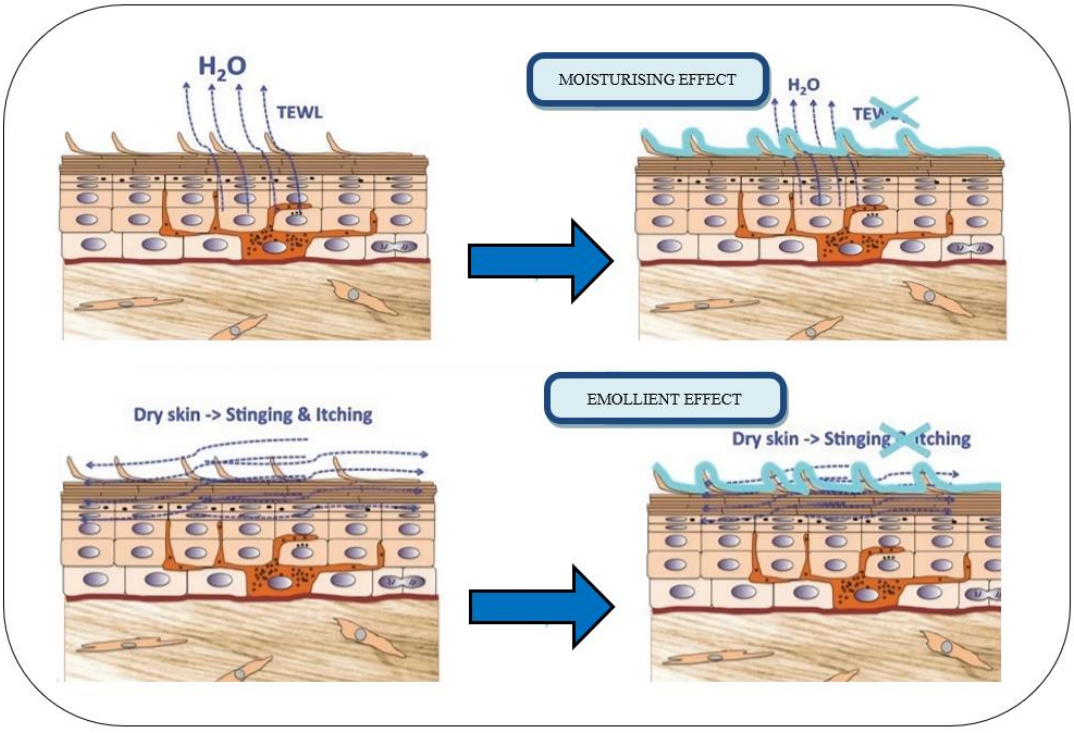

Figure 9. General mechanism of action of moisturizing cream in which water act as common evaporator from the deep skin layers from human body well known mechanism known as TEWL (Treansepidermal Water Loss), being producing naturally dryness providing easily removable surface protecting against harmfulmicroorganisms, debris, dusts or damaging controls.

Preventing dryness and brittleness flexibility loss after the applying of cream due to water content retain the moisture being determined by lipid barrier between them of each cell and also protected from itching and stinging for both normal and dry skin

type of nature. Thus, foreign substances get absorbs and prevents the skin from diseased [48,49].

9. Classification of moisurizing cream

Moisturizers as considered under cosmetic cream as well as in medicated products while applying to get prevent from various skin problems especially dry skin. But, moisturizers are constituents of active drugs and excipients use which help to improve the skin barrier function, clinical outcomes and prevent or eradicate skin disorders. The use of moisturizers popularly known from person to person personal experiences from their daily life cycle and because of their disorders cause, symptoms and severity that are being complex [50]. In addition, the products are now be claim to enhance the moisture content of the skin almost all basic constituents involved in creams form of formulations contain cream base ingredients having moisturizing property. These basic cosmetic effects act as moisturizers are been categorized based on the mechanism of drug action function as shown in **Figure 10** [51].

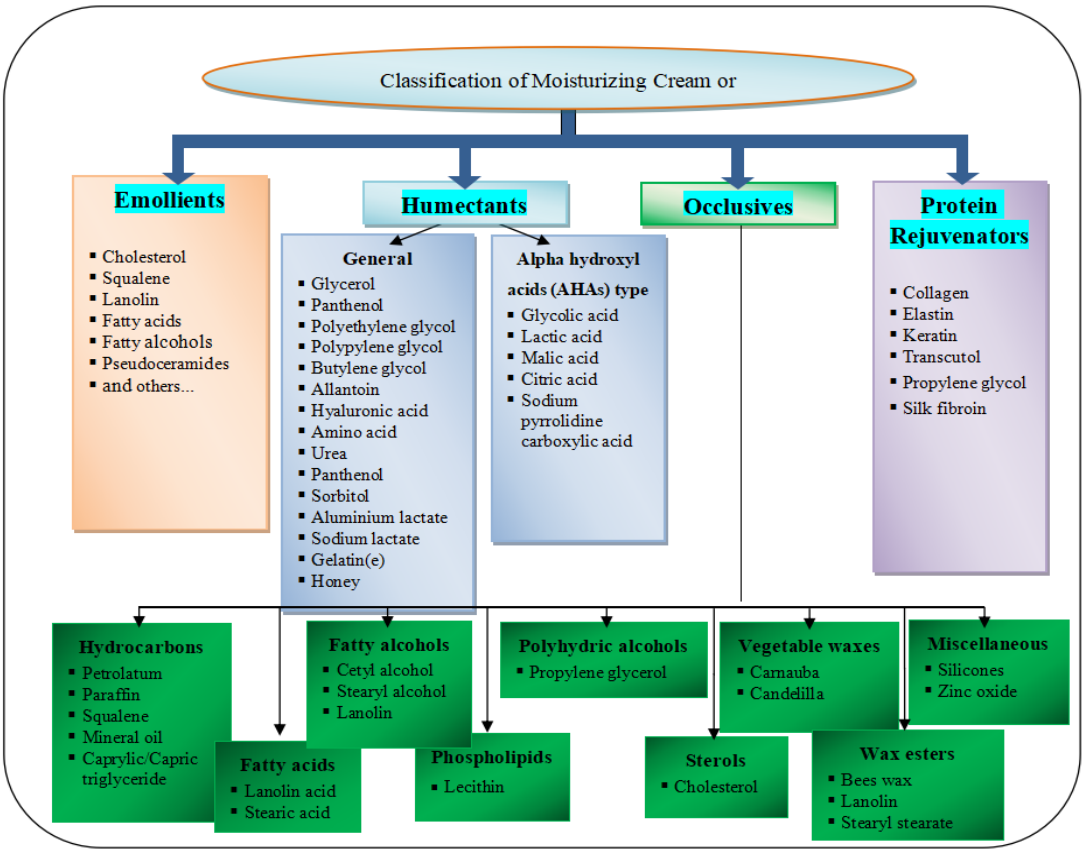

Figure 10. Classification of moisturizers categories with examples representing based on the activity of their constituent types based on their active ingredient mechanism effect.

Remember to note that in classification as given in **Figure 10**, Urea, Lactic acid and Malic acid includes under Exfoliants that also use as pre-moisture ingredient. Remember that some ingredients possess with multiple properties show on the skin [6,9,52].

9.1. Emollients

These agents are mostly composed of lipids and oils (water insoluble in nature) which moisten and enhance smoothness, softness, and suppleness 'feel' the skin via fills gap in SC. This lubricity texture of 'slip skin' promoting to satisfying consumers imparts softness and plasticity. Cholesterol and ceramides are categorized under lipophilic compounds being used in tropical creams. On dry skin, the keratin mass is removed due to rough feels cause, emollients were been used having moisturizing properties. Ceramides are the key lipid constituent and with neutral lipids both forming the broad laminated intercellular sheets that act as barriers for the environment under SC. Most of them are form of grease or oil based. They even work by enhancing ability to hold water and lubrication. But now, they integrated into liposomes to softer and smoother the skin texture [6,52]. Although, many of these agents might do not reduce TEWL and have little moisturizing function. It includes a variety of high-grade alcohols (such as cetyl and stearyl alcohols) and esters (such as octyl stearate, isopropyl myristate, cetearylisononanoate, oleyloleate, etc.) in which they both do not makes the skin dry [53].

Therefore, they improve the overall appearance and texture of skin. These types of fatty acids are helpful to get oxidized to eicosanoids, signaling with inflammation and influence the skin physiology [36].

The emollients have categorized into four types are dry, fatty, astringent and protective emollients based on nature as shown in **Figure 11**.

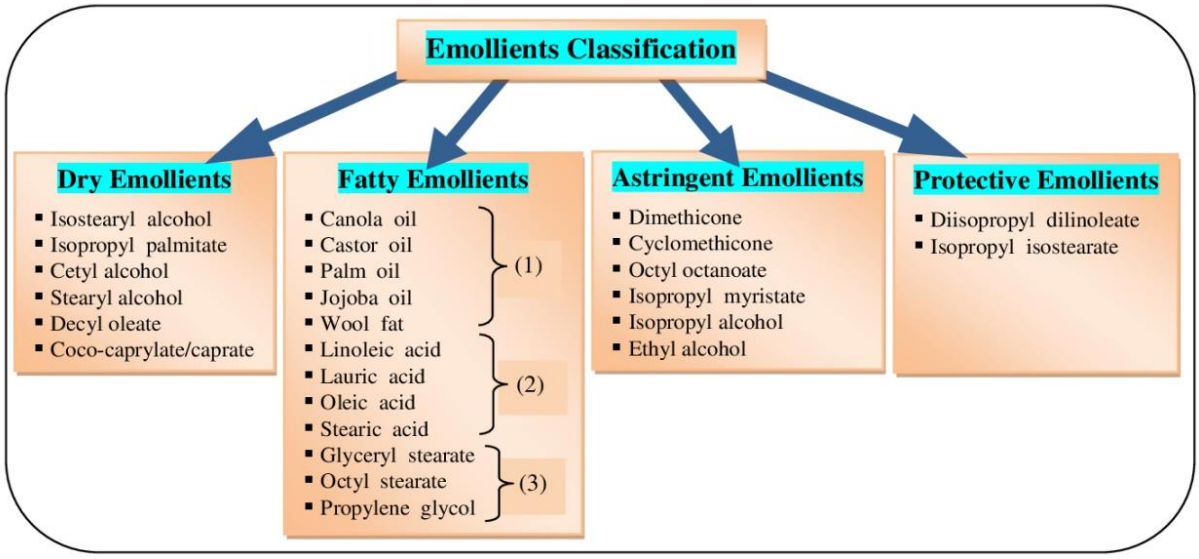

Figure 11. Classification of emollients. In which, (1) Fatty oils, (2) Fatty alcohols, (3) Synthetic category.
Note that Canola oil is specific to reduce sodium lauryl sulfate (SLS) irritation. In addition, Lanolin, mineral oil and petrolactum are also includes in both emollients and occlusives at same time [6,9].

Mechanism Action: Lengthy hydrocarbons derived saturated and unsaturated helping under membrane fluidity, skin barrier function and cell signaling which leads to better the texture of skin. Even combine with emulsifiers giving benefits for skin.

Indications and ADRs: Skin dryness, Roughness, Papulosquamous disorders and Routine skin care; Rarely contact irritant.

9.2. Humectants

These agents are mainly comprised of hydroscopic organic compounds mean to attracting the water from dermis and the epidermis sources under humidified conditions from the environment. They can easily absorb and retain the moisture below the SC towards SC having size 200–500 kDa. In this, Natural Moisturizing Factor (NMF) made the dissolved of low molecular weight (LMW) soluble hydroscopic substances such as Lactic acid, Amino acids and Pyrrolidone carboxylic acid which plays the main role for hydration of SC [6,53]. They are double-edged weapon enhancing water absorption due to TEWL due to this the sources lost easily environment. Among the humectants, water-soluble polyalcohol's such as Glycerine, Triacetin and Polyols that is most common traditional aqueous based gels moisturize and occlusive effects as such lack in creams in oilments and Urea, Lactate, Polypeptide, Hyaluronic acid, Sorbitol, Collagen and Elastin are also prefered. By this reason, they mostly combine with occlusive. Where, Alpha hydroxy acids and Trihydroxylated molecule glycerol are effective result treatment under superior lipid barrier resistant opposed to xerosis [44,54].

Mechanism Action: Mostly LMW particles with hydrophilic properties into the SC. By the help of along other components, the water content retains. They can cause water to evaporate into the environment (thus to prevent it occlusives involved to prevent TEWL) and helps to enhance epidermal barrier function and hydration levels to maintain.

Indications and ADRs: Xerosis and Ichthyosis; Irritation due to urea and lactic acid.

9.3. Occlusives

These agents are those physical blockers of TEWL under SC which creates the hydrophobic barrier around the skin, have the pronounced effect when applied to the slightly dampened skin and which contributing to matrix between corneocytes. These are naturally derived oils which are diffuse into efficacy. They act like sebum and natural lipids found in skin. They have different viscosities on the basis of molecular weight distribution. The most important compounds are Petrolactum, Mineral oil, Lanolin and Waxes consisting of complex combination of hydrocarbons. The hydrocarbon material is hydrogenated during the refining process to produce oxidation-resistant molecules that converts liquid to solid waxes which extending the long shelf life of these products [5,36].

Hence, Petrolactum is the best sealing lipophilic type of moisturizer involves intercellular spaces of the SC interaction internal occlusion effect providing increased barrier of water loss which is effective for dry skin patients. Among them, olive oil but is cosmetically less acceptable due to their greasiness whereas petroleum jelly is one of best moisturizers having water vapour loss resistance 170 times of it. The majority of most occlusives are limiting factor for greasy feel, odourable and potential allergenicity. Sometimes, it might show disadvantages such as in greasy feel, allerginicity and odor. Also, even though washing removed from skin after applied, the inhibition of moisture loss disappears. If it strong nature, then might cause microbial growth in the SC. Therefore, using of these agents based on the degree of

sealing should not lower moisture rate through epidermis by 40% or thus mixed with humectants [36,55].

Mechanism Action: An inert later formation via oils and waxes on the skin that physically blocks TEWL. So that TEWL reduce by forming a hydrophobic barrier film over the epidermis layer to prevent water evaporation via trapping it in skin's uppermost layers.

Indications and ADRs: Atopic dermatitis, Xerosis and Prevention of contact dermatitis; Cosmetically unacceptable, Messy to apply, Folliculitis (due to mineral oil causes), Contact dermatitis (lanolin), Acneiform eruptions.

9.4. Protein rejuvenators

They are facilitating drug delivery into skin disrupting the structure of SC which is only LMW proteins though to help by replenishing its essential proteins. They unlikely to occur due ti their large size to penetrate in dermis layer. The protein additives may provide temporary relief of dry skin by filling irregularities in SC. When its dryness shrink slightly leaving the protein film that appears to smooth the skin and stretches the fine wrinkles [46,56]. Naturally, these agents are the SC damaging barrier. However, care must be taken for choosing at optimal concentration for avoiding unwanted systemic drug absorption and skin irritation. These are act as solvents used as in combination for facilitating both partition and passage of drug through SC. In this, propylene glycol is the most thoughtful integrate hydrophillic region of packed SC lipids and enhancing solubility domain of drug. But at high concentrations (above 10%) of propylene glycol, it becomes irritating in nature [57].

Mechanism Action: An inert later formation via oils and waxes on the skin that physically blocks TEWL via following three mechanisms as to disrupting the highly ordered structure, interaction involvement or improving drug partitioning into SC lipid.

Indications and ADRs: Skin rejuvenation, Aging and Photodamaged skin; Contact dermatitis.

10. Benefits of moisurizing cream

They have several essential benefits except only moisten. So, the functions being provided by moisturizers:

10.1. Anti-inflammation

Various ingredients of moisturizers including glycyrrhetinic acid, telmesteine, ceramide dominant barrier repair lipids and filaggrin breakdown products have significant anti-inflammation properties. These actions include through various mechanism while blocking COX activity, reducing cytokines expression and relieving soothing effect on inflamed skin like dermatitis [22]. But in recent studies, anti-inflammatory agents are incorporated with emollients or humectants that provide the additional barrier to repair and control the dry skin. In case of mild to moderate occlusive emollient creams were recommended due to their thick barrier, lipid content variability and severity of disorders especially for atopic dermatitis. But, in severe case oilments been used due to their acceptance reduced (according to UK clinical experts) [21,22].

10.2. Antipruritic

Water-based moisturizers provide cooling impact on the skin surface due to water evaporation and some moisturizers contain menthol as an excipient, which also have cooling effect and less itchy symptoms [22]. Emollients with antipruritic substances as most times suggested. Hence, it should usually get treated either with moisturizers or with tropical and systemic immune suppresants. Although such therapies generally have good safety profile with better itch-specified medication choice required [58].

10.3. Antimitotic

Mineral oils-based are the therapeutic beneficial for dermatoses with elevated epidermal anti-mitotic activity such as psoriasis, since they have low-grade epidermal antimitotic characteristics. As they are considered as benefitter of cell death inducers. Thus, provides the skin fresh, slippery, neat and clean [22,58].

10.4. Wound healing

It has been shown that to hyaluronic acid accelerates the healing of wounds. Also humectants just in case of severe dry skin, humectants be suggested after with occlusive moisturizer such as petrolactum been recommended. But it may be critical to repair skin and improve its ability to retain moisture where emollients and lubricants involved [59].

10.5. Softness and smoothness

The consumers demanded to their skin smooth and soft that can be guarded by dead keratinocytes (corneocytes) layer on the surface of face. While using the emollient form of moisturizer can help the skin feel smoother and softer since folded corneocytes create friction when the layer of lipids is removed due to create friction when the hands are rubbed onto the skin surface [6,60].

10.6. Skin hydration

Scientifically significant moisturizers need to maintain the skin’s adequate moisture levels by slowing down and preventing water from evaporation from the skin surface hydrated via by TEWL mechanism. It enhances to reduce dehydration wrinkles and hydrate facial cleaning effects [8,61].

10.7. Photoprotective action

These days Sun Protection Factor (SPF) with variable of sunscreens are mixed with moisturizers providing addition sun protection. Many acne patients may or not considering to use as part of their skin care regimen which restoring a balanced barrier for long-term skin benefits. As being recommended to be use of both moisturizers and sunscreens in combination for Acne vulgaris treatment [61].

10.8. Enhancing quality of life

Having hydrated, smooth skin is essential to our social and psychological well-being life. Hence, the problems associated covered being with dry skin and due to their hydration mechanism moisturizers are adapted to perform an array function on skin

surface. As they are surprisingly sophisticated and equidistant between drugs and cosmetics. It brings challenges to scientists, germatologists, patients and non-patients/consumers [31,60].

10.9. Antimicrobial action

Microbial fights act against skin surface. Mostly in clinical study, the fungicidal and fungistatic agents are been mostly used for prevention of fungus such as *Malasseziafurfur*the common problem involve in atropic dermatitis disorder. Even, direct immunomodulatory effects have also been reported for the efficacy of this disorder [62].

10.10. Potential to deliver materials to the skin surface

A variety of emulsions, including double emulsions, micro or nano emulsions, gel emulsions and quick breaking emulsions have been used in skincare products as moisturizer delivery agent. Different moisturizers have different properties that are being altered by combining them with excipients that can efficiently penetrate skin tissues enhancing skin moisture [61].

11. Moisturizer applying manner form

Applying moisturizers at the appropriate time and with appropriate techniques will yield it best for optimum results via collecting moisture from the environment or underlying layers of skin surface aside from humectants and hydrophilic matrices. After taking a bath, dabbing the skin or by rubbing a wet cloth (sponge bath) skin should be used to moisturize it. Applying moisturizer rub softly and in direction of hair follicles should come after massaging it in on both palms. It is important to thoroughly explain application techniques to patients or users in order to preventing oil folliculitis (hair follicle swelling) characterized by vigorous handling via rubbing [7,22]. Use several times, if your dry skin nature patients help to reduce the oily secretion period from skin. Moisturizers being involved of humectant agents evaporate moisture exposing cold, dry air after being applying on skin. Recommend use of product for 30 min before exposing cold and dried feel. If skin exposed of dry air immediately recommend the use of occlusive agents containing moisturizers which feel good and suppress water loss immediately [63].

The distribution of moisturizers varies on the vehicle type as compared to formulations with lower viscosity and higher volatile components, thick oilments have more uniform distributed of constituents. Unlike lotion and tinctures, creams and oilments are easier for APIs to transfer to surrounding nearly surfaces [52]. After application, ingredients may retain on the skin surface, penetrate into the skin, absorbed, be metabolized or leave the skin, disappear from the body by evaporation, sloughing off or by contact with other materials. Just only 50% moisturizers were still remained on the skin surface after 8 h. Therefore, suggested application frequency varies between 1 to 3 times per day, depending on severity of dryness recommended [6–8]. It could take some trial and error to determine which moisturizers are best suitable for a particular person. With the exception of humectants and hydrophilic

matrices which are the most often used occlusive oils applied on most skin types absorb and retain water from atmosphere or underlying skin [6,63].

12. Adverse effects of moisturizers

Even when used over longer duration of time on broadly surface areas, moisturizers are rarely linked to health problems when compared to other prescriptional drugs. As various products, may trigger skin responses in sensitive areas of few individuals, there are varieties of discomforts connected with moisturizers are frequently encountered. The most common adverse/side effect is skin irritation which might be a sensory reaction or subjective feel sense with or without indications of inflammation [23]. Skin irritation is a sensory reaction or subjective sensation with or without signs and symptoms of inflammation which is the most frequent adverse effect while keeping appropriate in selecting moisturizers from discomfort preventions clinically checked. Also, natural herbs (Chinese herbs) are adulterated with corticosteroids cause serious side effects in modern times. Various skin discomforts from tropical formulations encountered as skin reactions at sensitive regions in some individuals. Even, facial creams are more sensitive than other body skin results less efficient barrier with small number of SC cell layer with large follicular pores [7,22].

When allergic or irritant effects caused by moisturizers suspecting repeated patch test or open patch test diagnosis takes place. Even stability of moisturizer ingredients is being treated as more important and cumulative amount frequently applied for whole body being considerable. It is important to choose products within safe ingredients within safe concentrations due to enhanced absorption. If consumer might suffer from apotic dermatitis (common skin disorder), then damaged skin barrier or immature skin problems (paediatric to adults), then moisturizers is the best option. Even some causative agents may include preservatives, fragrances and other such additives are important indicators of such side reactions. Due to long-term benefits effects, carcinogenesis possibility emerges from preservatives or anti-fungal agents, dermatologists being tackle such basic issues [52,64].

13. Therapeutic use of moisturizers

Moisturizers often several wide benefits for numerous dermatoses linked to dry skin-associated. Complex interactions between individual and environmental factors lead to dry skin condition. Under low environmental temperatures, chemical exposures, low humidity, aging, psychological stress, microorganisms, atopic dermatitis and eczemas are among the contributing factors [22].

A good moisturizer being applied gently gets restore skin’s normal barrier function. Moisturizers being involves with the skin type in which for dry skin type such as oilments or oily cream formations whereas for oily type skin lotion and water based moistures are been recommended. The body part prone to small amount cream having content of occlusive agents should be selected who are natured from dry skin even beneficials during winter season [52,65].

In past, moisturizers give the skin as wetting property of NMFs and heals the sebum function. Recent studies prove that restoring and strengthening of skin barrier function refer inter-keratinocye lipid components involves ceramides and lipids

lamellar structure functioning as skin barrier and maintain homeostasis. Even several new modificatins are being highlighted for own lipid layered structure be well-fused to the SC lipids. But some synethic ceramides or similar pseudo-ceramides precursors that helpful in enhancing synthesis [65]. Moisturizers in form of physiological lipid compounds known to reduce damage of skin barrier function caused by external steroids, so the expected to being increase as therapeutic adjuvant [63].

14. Positive and negative consequences

Certain positive consequences are present as follows [36,66,67]:

1) The main effect of moisturizers is to enhance the skin dryness without any side effects.
2) It reduces the further changes of skin problems or disorders.
3) Its emollient properties being soothe and soften skin.
4) This moisturizer helps to fight against wrinkles, blemishes and helps skin stay younger.
5) Less greasy compared to other semi-solid formulations.
6) More spreadable and less greasy than oilments resulting enhanced patient compliance.
7) It is perfect end to a hot shower.
8) Within small quantity, it is very useful as compared to synthetic cosmetics.

But few, negative consequences are present as follows [35,66.67]:

1) Difficult to hide taste and odor.
2) Require small plasma concentration of drug action.
3) May not compile with every person and may cause allergy or irritant skin problems.
4) Risk of contamination is high due to less hydrophobic agents use than other semi-solid preparation.
5) Less occlusives and hydrating decreases percutaneous drug absorption.

15. Some common brands of moisturizing creams with its claim

There are some common brands of moisturizing creams with its claim (as shown in **Figure 12**):

Figure 12. Some famous brands of moisturizing creams.

16. Preparation of moisturizing cream

This is the preparation/method for Water-in-oil type emulsion. For this at first, all the formulation of polyherbal moisturizing cream was to collect and arrange different glasswares (such as beakers, spatula, measuring cylinder, petri dish, etc.) and equipments (such as weighing machine, spatula, heating mantle, etc.). After that, the pure extracts of Aloe vera gel and Lycopene were taken previously from their botanical sources as well as other ingredients were taken. W/O type emulsion formulation being prepared by make using of two different phases with continuous agitation were as follows while applying under different formulations pattern shown as per given in **Table 1** [66–68]:

Table 1. Formulation composition of moisturizing cream [68].

Phase. No.	Ingredients	Quantity/Amount for 200 gm (% W/W)	Role of Ingredients
Phase 1.	Aqueous Phase:		
	Aloe vera gel	3.8	Moisturizer, Anti-inflammatory, Anti-aging, Wound healing, Antioxidant, Reduce acne & pimples, Burns healing.
	Lycopene powder	3.8	UV-radiation adsorber, Anti-inflammatory, Anti-microbial agent.
	Powdered borax	15	Alkylating agent, Stabilizer.
	Distilled water	q.s.	Diluent / Vehicle.
	Vitamin C	3.5	Antioxidant, pH Stabilizer, Skin protectant.
Phase 2.	Oily Phase:		
	White Bees Wax	15	Emulsifying agent, Humectant, Stabilizing agent, Thickening agent.
	Cocoa Butter	6.8	Protective against oil-nature, Protective barrier of skin, Elasticity improver, Smoothening agent.
	Emulsifying wax	6	Non-ionic Surfactant.
	Coconut oil	1.5	Emollient, Anti-acne, Reduces dark spots.
	Almond oil	1.5	Moisturizer, Protective layer skin, Anti-wrinkle, Anti-itching.
	Eucalyptus oil	1.5	Lubricating agent, Antioxidant, Disinfectant.
	Vitamin E	1.57	Antioxidant, UV-radiation adsorber, Emollient.
	Vanilla essence	12	Fragrance/Perfume.
	Ethanol	0.025	Preservative & Anti-microbial agent.

1) The SOP (Standard Operating Procedure) should be while cleaning and washing of all the apparatus and chemicals.
2) In a separate phase, all ingredients were accurately weighed.
3) Phase 1: Oily phase consisted by melting all the solid/waxes ingredients and surfactant by indirect heated up to 75 ℃ ±1 ℃ then completely mix while add with all of the oils.
4) Phase 2: At the same duration, aqueous phase consisting of borax which dissolved in distilled water was heated at same temperature and then the Aloe Vera gel extract, Lycopene extracts and Vitamin C was added in it.
5) Add the phase-1 into the phase-2 gradually, still hot while with continuously rotating to stir the wax and oil mixtures until the complete addition takes place.
6) During this stirring time period, add few drops of essence and preservative were added while providing the mixture with nice fragnance effect impact under formulation.
7) After 5 min of continuous stirring, remove from the heat to achieve for complete homogenization and mix until it becomes moisturizing. By adding additional wax, the cream may be made thicker than other creams.
8) This all similar components and procedure steps described above were also used to produce cream base but without Aloe Vera gel and Lycopene extracts (which are active components). It's simple W/O basis was chosen to ensure that it wouldn't affect the evaluation of Active's moisturizing properties.

Note point: Vice versa for the preparation of cream when it comes to an Oil-in-Water emulsion type cream but the content of the oil and waxes will be the greater as compile with the water content less in quantity.

17. General ingredients used in moisturizing creams to formulate

The needed ingredients which are used for the manufacturing of moisturizing creams as follows:

17.1. Raw water

The most significant and frequently utilized the raw ingredient in any formulation of cream. These are most affordable and obvious direct excess material. Water is a solvent used under skin creams to dissolve other components. Toxins, pollutants, microbes, and other contaminants must not be present in the water used under cream's preparation. Even, the amount of water required in the formulation for Water-in-oil and Oil-in-water types of emulsion depending on the amounts of both oil phase and water phase manually [69,70].

17.2. Fats natured oils

They are number of derived from mainly comprise of an essential portion for creams formulation. Even helpful in perfuming agent, preservatives, etc. Where oil mainly of two types minerals and glyceride oils are as follows [70]:

17.2.1. Mineral based oils

It is made up of hydrocarbons from the petroleum oil, which is heavily refined, clear, odourless and can be frequently used in cosmetics. It might cause in frequently results in allergic reactivity and perhaps be unable to solidify the block skin clog pores. It is inexpensive, light weight, reduced water loss from the body and moisturized the body. e.g., Liquid petroleum, Light liquid paraffin, Heavy liquid paraffin, etc.

17.2.2. Glyceride based oils

It is essentially derived from vegetable and even animal oils origins which are form surface barrier of skin, rate reducing water loss and maintaining its plumpness of the epidermis. It can also be used to increase the thickness of the lipid or oil components of creams or other personal related products. e.g., Arachis oils, Almond oils, Sunflower oils, Coconut oils, Germ oils, Cocoa butter fat, mutton tallow, lard, etc.

17.3. Waxes

It acts as an emulsifier or ester component of fatty acids which may involve for cream preparation due to its prevention the separation of liquid and oil components in an emulsion and have high melting point. They are also used thickness enhancing liquid part and gets bind on skin's surface. e.g., Beeswax, Carnabua wax, Spermacepti, Ceresin, etc. [71].

17.4. Fats

It acts as a thickner where it mainly obtained from plants, minerals and even animals origin. They are produced up of glycerin and higher fatty acids combinations.

Depending on the processing utilized, they can saponifing into glycerin, fatty acids or soap formation. Lauric, Margaric, Palmitic, Stearic and Saturated groups are most prevalent fatty acids, although Oleic acid is the frequently used liquid unsaturated fatty acid [70,71].

17.5. Active/Main ingredients

It mainly includes Emollients, Humectants and Occlusives and Protein rejuvenators (rarely involved) agents that are main ingredients of moisturizing creams compulsorily used as ingredients has been previously discussed with examples.

17.6. Vitamins

They are essential for preserving the skin's and the body's physiological function and the skin. As they are tropically used to treat and prevent changes related to photoageing, involves with hyperpigmentation treatment and with various other skin benificial elements present. They are generally used in formulations of creams such as Vitamin A, B_1, B_3, C, D, E, etc. [72].

17.7. Antioxidants

It is also used to protect the alteration exposed to oxygen that inhibits the oxidation of other molecules. These are occasionally being used to inhibit rancidity in tropical vehicles containing from unsaturated oils and fats which are common emulsion-based creams. These agents are being neutralizes free radicals, unstable oxygen molecules which breaks down skin cell refer to wrinkles. They inhibit inflammation leading to collagen depletion and protects against photodamage and skin cancer. e.g., Vitamin C, Vitamin E, Ascorbylpalmitate, Butylated hydroxyanisole, etc. [73].

17.8. Thickeners/gelling formers

These are influential tropical vehicle viscosity, skin retention and penetration of drug takes place. In this, mostly naturally and synthetic derived based thickener involved. However, naturally derived represents those polymers involved in absorbing water causing them to swell up and enhance vehicle viscosity. Whereas in synthetic derived being involved only for lotions and creams. e.g., Guar gum, Gelatin, Hydroyl ethyl cellulose, Cetyl palmitate, Ammonium acryloyldimethyltaurate, etc. [36,74].

17.9. Emulsifiers/stabilizers/solubilizers

They are used to reducing the surface tension of the cream to make the nature more stable and plays a significant role in the stability of tropical vehicles by keeping different substances (such as oil and water). These agents have hydrophilic and lipophillic part where the structure gets absorbed onto the oil-water interface provides protective barrier around the dispersed medium. The emulsifier may also create a film over one phase to another form globules which repel each other in such a way that this repulsive force remains suspended and dispersed medium. In case of moisturizing cream, non-ionic surfactants are used for compatibility with other surfactants. e.g.,

Oleic acid monoglyceride, Emulsifying wax, Polyoxyethylene lauryl ether, Coco fatty acid diethanol amide, etc. [36].

17.10. Stiffeners

These are the main structure-forming additives excipients in tropical semisolid formulations such as in creams. They even possess with high lipid content forming a protective occlusion barrier on skin from harmful substances and keep skin hydrated. Even they also used as emollients to smoothen, soft and lubricates the skin to prevent TEWL. e.g., White soft paraffin, Liquid paraffin, Lalolin, Bees wax, Carnabua wax, Cetyl alcohol, Isohexadecane, etc. [75].

17.11. pH adjusters/modifiers

They are rarely needed components in any cream formulation, but only to adjust or modify the end of manufacturing or preparation throughout their shelf life. However, for skin compatibility nature via for consumers and for the product's functionality of physical, microbial stability and response effect of skin reaction. e.g., Borax, Citric acid, Triethanolamine, etc. [36,70].

17.12. Colors

The colors are predominantly come from natural sources and even have also been synthesized in laboratories to provide considerably more high vibrant colors without requiring for gather plants harvesting in wild. Its requirements is less due to creams auto-color formation. e.g., Turmeric, Saffron, Indigo, etc. [70].

17.13. Perfumes

They are substances that impart scent or order to odour includes sweet and pleasant which helps to attract the consumers or clients with the great population. e.g., White blossoms, Rosy dreams, Orange blossom, Lavender, etc. [68,76].

17.14. Preservatives

They are necessary in cosmetic formulation, shipment, storage and consumer usage to get free from microorganisms and contamination alteration. Where items are successfully preserved via synthetic preservatives at low concentrations. It must be active against a wide spectrum of microorganisms its selection be based on various factors such as formulation compatibility, toxicity, irritancy potential and the site of vehicle. e.g., Ethanol, Formaldehyde, etc. [36,70].

18. Evaluation parameters of skin cream

As to accept the moisturizers cream by different nature of skin type people was to be follow the evaluation test to get uplit of their desired or adapted for use. In this various identification of tests can be done as follows:

18.1. Organoleptic appearance

This refer to the formulated manual emulsion of the cream's physical characteristics was to be analyzed/observed visually by its color, odor,

texture/consistency and state were carried out. The cream's long lasting color and roughness was measured and graded by its physical look via naked eyes [68]. These parameters helped in visual identification of cream. This must be evaluated in order to study the stability, suitability for the skin and establish various ranges for the moisturizers. They also measure the consumer acceptance and preference [77].

18.2. pH Determination (Calibrated)

By mean, the pH of all moisturizing creams was always should be get under the range of between 4.5 to 6.5 which was good for skin pH & also it fulfills the criteria under standards. In this, a glass electrode as reference electrode with a digital pH meter, the potentiometric method was used to determine the pH value of a solution. According to manufacturer's instructions was followed for using it where the equipment at first standardized by calibrated using buffer solutions of pH 4, 9 and 7. Next, in an appropriate beaker, the pH of the 10% w/v cream suspension was taken which dissolved in demineralized water (as solvent) at room temperature. The pH was determined after the electrodes submerged in the solution [78].

18.3. Viscosity

By using Brookfield Viscometer with a helipath stand which determined rheological studies of acertain viscosities of all moisturizing creams. The sample were being taken prior to taking dial reading 25 ℃ temperature using spindle No. 63 at 2.5 r.p.m. allowed to equilibriate for 5 min. Per rate of speed, the corresponding viscometer dial reading recorded. Viscosity in centipoises obtained by directly multiplication of dial readings by factors listed on its Brookfield Viscometer catalogue include with the instrument [70,78].

18.4. Homogenicity

This method is being helpful to know the nature of cream is in usual phase or denature. In this via applying 1 gm preparation assessed onto a clean object-glass showing a homogeneous arrangement without any appearant grain patterns that should spread evenly in all creams. It was also being determined whether there be any unmixed particles or lumps in the initial skin feel involves stiffness, grittiness and greasiness [78].

18.5. Phase separation

This mainly refer to the state of phase after for longing is supporting or not in formulation. In this after 24 h of prepared formulated cream, the oil phase and aqueous phase separation visual takes place which was then poured into an appropriate wide closed mouth, store and kept away from direct light at temperature 25 to 100 ℃. Every alteration in phase separation was noted and examined [79].

18.6. Spreadability test

This test is being taken for the perfect outcome of cream speed is checked, where faster the speed to get faster effects. In this test, the samples assessed using the following technique in which adequate amount of 0.5 gm sample formulation was

setup inside a pre-marked 1 cm diameter circled glass plate which was placed. For 5 min, a weight of maximum 500 gm could rest on the upper glass plate. It was observed that the test formulation spreads via enhancing the diameter [70]. Thus, all values are taken and put in the formula to get where the cream relates:

$$\text{Spreadability} = \frac{\text{Weigh tied to cream via upper slide (m)} \times \text{Glass slide lemgth (l)}}{\text{Spreading cream time taken duration (t)}}$$

18.7. Washability/removal test

It was carried out by ease small amount enlarging the elimination of formulated creams where it was administered under running tap water were allowed for gentle observation under applied part or region [70]. To get the hands get easy to clean.

18.8. Irritancy/irritability test

In this, skin nature with the skin touch test takes place in which a single irritant or alergic feels. Then it must get discard mean if it is not compile of your skin or some other issue. On the left-hand dorsal region, make an area of 1 cm^2. Next, the prepared formulated creams applied on that specific part were time recorded. After that contact skin were being examined for itchiness, erythema and edema effects. If any irregularity intervals within upto 24 h, data must be noted and examined [80].

18.9. Centrifugation test

For longing of cream this step is has been taken. This centrifugation involves 5 to 10 gm of sample under 30 min at room temperature at 3000 r.p.m. After following centrifugation process, phase separation which indicates formulation instability by the presence of caking, coalescence and flocculation. In this, all creams being performed for the sample of base and formulation kept at different storage condition at an interval of 28 days period of time. Meanwhile, evaluated physical (creaming and phase separation) and organoleptic (color, feel, look & thickness) attributes in interval [81].

18.10. Light test

In this evaluation, light bulb under photoperiodicity system alternates between 16 h. of light and 8 h. of dark regions while was housened in clear plastic containers. Once the exposure period was up, the samples examined in any alterations in their physical characteristics includes appearance nature, clarity, colour while adding liquefication. As negative impact such present found in color shift or such phase separation known to be product instability [9,68].

18.11. After feel test

After applying all creams, emolliencyslipperiness with residue amount left or fixed amount of cream effect at the skin were beingnoted and examined [82]. So that best creams can be find out.

18.12. Type of smear/film determination

After applying all creams, the kind of film/smear type formed that developed on skin’s surface being noted and examined via human volundeer for getting observe with

its greasiness and behavior on the skin, if the smear was only or greasy like nature [70,80].

18.13. Density

The primary method used for measuring product density by a pycnometer which can be determine by using empty pycnometer weight with cap, fill it with sample until to full and then weighed repeatedly. The density value now gets calculated via by using following given formula [9]:

$$\text{Sample Density} = \frac{\text{Sample weigh (gm)}}{\text{Water weigh (gm)}} \times \text{Water density (d/mL)}$$

18.14. Sensitivity and its exposure irritation test

This effect is being studied to know about the cream use under sunlight or not. In this, cream was being prepared was applied on a hand under 1 cm area of skin diameter exposing sunlight rays since 4–5 min. Even claims that the cream "self, no permissions need natural non-toxic and safe use components that render making exceptional" when applying it to the skin of volunteers (Puja Saha, Supriyo Das et al.) [80].

18.15. Dye test

In this evaluation, it includes combining of cream with scarlet red dye help to know about emulsion type of creams. Where, drop is putted onto the cream slide covering it with a slip and uses it with a microscope for examination the result. If the situation occurs for O/W type cream, when disperse globules looks in the red and ground colourless. As opposite situation for W/O type cream, when the disperse globules appear red where the ground colourless [68,70].

18.16. Acid value determination

The acid value is the measurement of the amount of free acid in fats or oils that causes rancidity upon exposure to heat or light. In this, 50 mL of precisely weighed equal parts alcohol (ethanol) and solvent ether (diethyl ether) are mixed with 10 gm of the cream is dissolved in them. Then following, the flask connected with reflux condenser and heated progressively until the sample dissolves entirely. After trembling 30 mins, 1 mL of phenolphthalein is added and titrated with 0.1N NaOH until a faintly pink shading appears [9,68]. Thus, all values are taken and put in the formula to get the cream relates:

$$\text{Acid Value} = \frac{\text{0.1N KOH solution (mL)} \times 5.61}{\text{Cream weigh (gm)}}$$

18.17. Saponification value determination

The saponification value is a measure amount of saturation, with higher values indicating free fatty acids chain in the glycerol bond or esters in a sample which affects the formulation's stability, pH and cleansing properties should be appropriate. In this, 1 ml of phenolphthalein added with previously 2 gm of cream that has refluxed for 30 mins with 25 mL of 0.5N alcoholic KOH, then immediate titration takes place with

0.5N HCl. The readings being denote as ‘a’. Again the process another time, while leaving out the investigating omitting the sample examined that investigating omitting sample being examing the resuted reading denoted as ‘b’ [9,68]. Thus, all values are taken and put in the formula to get the cream relates:

$$\text{Saponification Value} = \frac{(b-a)\times 28.05}{\text{Cream weigh (gm)}}$$

b = Volume of titrate in omitted condition (no cream involved) and, a = Volume of titrate (cream involved).

18.18. Hard and sharp edged abrasive particles

Take the sample cream of about 15 gm on plain of paper. Spread the cream containing hard and sharp edge abrasive particles on paper via help of felled finger. By which, that cream formulation must not contain abrasive particles that are being hard to touch by fingers [78]. This must be discards if fails because it may be caught with foreign dust, dirt or expired.

18.19. Total fatty substance (TFS) content determination

In order to do, precisely weigh 2 gm of sample into a conical flask filled with 25 ml of dilute HCl, under reflux condenser being attached into flask, boils the contents until clear solution appears. After pouring contents into300 mL-separating funnel, less it to cool down at 28℃. Then, use portions of 10 mL each with 50 mL of Petroleum ether to rinse the conical flask. Fill the separating funnel with petroleum ether give rinse into that funnel under shaking and wait until the layers separate. Shaking off the aqueous phase twice and 50 ml portion Petroleum ether. Petroleum ether extracts are all merged and rinsed them with water until acids free (knowing by dropping methyl-1-orange indicator solution). Poured the Petroleum ether extracts via filter paper that has previously dried at a temperature of 90 ± 2 ℃ and then weighed and filtered extracts through Na_2SO_4 (Sodium sulphate) into conical flask. Use petroleum ether to clean Na_2SO_4 on the filter, then mixed cleaning the filtrate. Remove the petroleum ether and dried it the remaining in the flask under temperature 90 ± 2 ℃ while maintaining constant mass. The acceptance measurement range is given according to BIS that not more than 5% by mass requirement [83]. Thus, the product value and previous product value putting the values in the formula:

$$\text{TFS (\% by mass)} = \frac{\text{Residue mass of cream } (M_1 \text{gm})}{\text{Material mass taken for test } (M_2 \text{ gm})} \times 100$$

18.20. Non-volatile/residue content determination

In this measurement, accurately weigh 5 gm of sample cream which must be cleaned and dryed of large squat weighing bottle and then heated on a steam bath under an air jet for 30 min. Next, continued it at 105 ± 1 ℃ in an oven of 2 h for dry to constant mass which was cooled in a desiccator and weighed. So, the acceptance criteria range is given according to BIS that not more than 10% by mass requirement [83]. Thus, the product value and previous product value putting the values in the formula:

$$\text{Residue (\% by mass)} = \frac{\text{Residue mass of cream } (M_1 gm)}{\text{Material mass taken for test } (M_2 gm)} \times 100$$

18.21. Ash value determination

To eliminate adulterant the measures are taken. In this measurement, the amount of produced ash serves as a gauge for how well the demineralization (DM) process eliminating $CaCO_3$ as indicator of effectiveness. The involved weighing 5 gm of each formulation into porcelain dish and heating it for an hour on a steam bath under a air jet. Next, a glass stirring rod was combine used with 1 gm of cellulose powder ash-free natured. The dish was being placed in a muffle furnanceheated to 600℃ where it then noted and examined [77].

18.22. In vitro occlusivity test (F)

To finding the water nature of cream nature in this test was taken. In this, each beaker having dimentions 3.2 cm of diameter and 4.6 cm of height was the tests conducted via placing 10 gm distilled water were in each beaker opening end was sealed with Whatman filter paper (0.45 pore size) that had 200 mg of sample equally distributed on upper surface. Thus, these beakers were kept at 37 ± 2℃/607 ± 5% RH for 48 h. by calculating the water flux samples of all formulated creams prototype and a negative control filter paper left uncovered studied were examined water flux [32]. All values were been taken and putted comparative product value in the given formula:

$$F\ (\text{in } \%) = \frac{A - B}{A} \times 100$$

A = Water flux via uncovered filter (percent water loss) and, B = Water flux via filter when covered by test preparation (percent water loss).

18.23. Psychometric/preference analysis

The formulated creams were being differentiated involving the sensory evaluation methods were degree are being assigned decided by high ranking score was examined as per achieved based on Hedonic scale given in the **Table 2**. The Colour, Texture, Wetness, Odour, Thickness, Spreadability, Absorbency, Gloss, Slipperiness, Firmness Stickness, and even Skin sensation are all parameters involving under psychmetric/preference analytical study takes place [9,68].

Table 2. Hedonic scale scoring board for grading the creams while dispencing formulations of moisturizers [33].

Grade	Score
Extremely liking	8.5–10
Between both extremely and medium natured like	7
Medium/Neutral	5.5–6
Between both medium and dislike nature	4
Highly dislike natured	1.5–3

18.24. Test for freeze thaw

In this, all prepared creams involve freezing at low temperatures before bringing them to room temperature. The 5 times repeated cycle, changes were noted and verified through via visual manifestation [68].

18.25. Thermal stability test

In this, placing the prepared sample creams in glass container and tap until it settling down with the aid of spatula. Filling the two-third volume of bottle, inserting plug and tightens lid. Now, maintain the filling bottle directly under incubator while measures at rate of 20℃, 30 ℃ and 40 ℃ for 48 h. was determined according to Bureau of Indian Standards (BIS) and Indian Standard Guideline (ISG) in which as such no oil phase breaking takes place [68,84].

18.26. Cytotoxicity test

In this, we assessed neutral red uptake of 3T3 by measure absorbance after 2 h. incubate the samples. The evaluation that has been performed under various concentrations in which values counting under IC_{10} and IC_{50} can be counted by using formula of Cell viability (CV). This method primarily confirmed of 50% CV concentration of IC_{50} from an in-vitro basal cytotoxicity assay. Thus, there at 100% viability shows non-cytotoxic whereas 0% viability shows maximum toxicity [60]. All values were been taken and putted comparative product value in the given formula:

$$CV=1-\frac{OD_{Sample}}{OD_{Control}}\times 100$$

18.27. Phototoxicity test

Using the same concentration o cytotoxicity test, we evaluated 3T3 neutral red uptake. After being an exposed to radiation (UVA+) at specific amount periods of time to being achieve dose 5 J/cm^2, and the same rated without concentration in light absence (UVA−). Data are being examined using Phototox® measured under certain wavelengths. Thus, on the basis of validation study the calculated Photo Irritation Factor (PIF) and Mean Phototoxic Effect (MPE) under predictive parameters as listed on **Table 3** [60]:

Table 3. Results table of PIF and MPE interpretation.

PIF and MPE	Phototoxicity potential
PIF < 2 & MPE < 0.1	Absent Phototoxicity
PIF < 2 & MPE > 0.1 & < 0.5	Possibility Phototoxicity
PIF > 5 & MPE > 0.15	Present Phototoxicity

18.28. In vivo test

In this, the safety evaluation of formulation being carried out to normal skin of upper back for 48 h by applying to skin is measured on the protocols followed under International Contact Dermatitis Research Group. After informed consent filled up, they were being accomplished by 18 volunteers aged 22–45 years. According to the

exclusion and inclusion criteria, volunteers type II to IV Fitzpatrick skin type selection where responses are being analyzed after 30 min, 24 h and even 48h product is eliminated from skin surface. The consideration safe of formulation not exhibit papules edema or erythema to deemed volunteers [60].

18.29. Anti-microbiological study

Tropical formulations are essentially broad-spectrum, non-resistant via promoting agents against various microbes that are useful in dermatology preparations infections are frequently combined. Due to the fact that formulations with microbial compounds as active moiety ability to preventing growth of microbial agents have been optimized antifungal property studying under observation with all others developed creams. Prior to anything else that extract's MIC (Minimum Inhibitory Concentration) was analyzed opposing to *Candida albicans* (type of fungal stains) by using agar disc-diffusion screening assay were the zone of inhibition were noted and recorded [85].

18.30. Accelerated stability studies

On the compilance with ICH demands, created formulations received the accelerated stability analysis subjected to testing under duration of 2 weeks conduction. The most stable formulations were designed and recorded specifically at room temperatures of 25 ± 2 ℃ and 40℃ ± 2 ℃. They exposed to two relative humidity levels, at 60 ± 5% RH and 75 ± 5% RH. On the 7th day, the kept creams both at room and high temperature and witnessing evaluated parameters [9,80].

18.31. Electrical conductivity

This measure was taken to know about the cream composition with the components or additives along with main drugs and identifying features of fermentation states also. Basically, values of electrical conductivity of freshly prepared emulsion which kept at different storage conditions were monitored at 28 days determined by Digital Conductivity-Meter. If there is no change then the value is always remained zero [81].

18.32. Skin moisture content or moisturizing property determination

The skin moisture content was being measured by Corneometer also known as Capacitance method where SC is measured with a skin capacitance meter (CM 825). The instrument determines the moisture content of the superficial epidermis region, down to depth amout 0.1 mm as such values shows in arbitary units. This was done on the inner forearm of the selected volundeer previously creamed. 7 such blocks were drawn 2 × 2 cm on that forearm, for blank (skin moisture), its base (control), 1%, 2% and 3% with active effects applied cream. The probe was placed vertical marked on skin surface with little pressure for a second which being displaced by Corneometer noted as blank. and then analyzed on days 7, 14, 21, 28, 42 and 56 with the help of its probe due to this percentages changes measurement show on skin moisture. After that average was taken were the plotted graph represents [84].

18.33. TEWL (trans epidermal water loss) determination

The net skin was measured by the aid of Tewameter before applying of cream and its base and then analyzed on days 7, 14, 21, 28, 42 and 56 with the help of its probe due to this percentage changes measurement show on TEWL [81]. In this, 10 repeated baseline measurements were performed on volar forearm with the TM Hex and TM 300. The additional seven anatomical locations are being measured by TM Hex. On volar forearm, added values to the SC hydration were assessed. Where, for cosmetic application such as creams for the last 24 hrs. The study being carried out by respecting the guidelines and intending to show a non-inferiority of the tewameter TH Hex estimation for the needed sample size based on published comparative studies. The study was performed under declaration of Helsinki [86].

19. Conclusion

Moisturizers is a semisolid or solution for the dry skin due to the enhancing of skin's hydrating properties and mechanisms such as emollients that prevents water evaporation from skin surface, humectants that attract water and smeared to the skin surface, occlusives that being blocks TEWL to penetrates water level to the SC or the rejuvenators of proteins that rarely used low proteins weights by replenishing essential needs and physically blocks TEWL at the SC surface. Within the formulation of research and development of moisturizing creams purposes are repeatedly gives profits and satisfaction for the clients, consumers and even patients. Moisturizers being involves with the skin type in which for dry skin type such as ailment or oily cream formations whereas for oily type skin lotion and water based moistures are been recommended. Petrolatum is the best sealing lipophilic type of moisturizer involves intercellular spaces of the SC interaction internal occlusion effect providing increased barrier of water loss which is effective for dry skin patients. The findings of evaluations conducted for once mentioned moisturizig ingredients need to be demonstrates an improvement under sophisticated criteria considered for moistening effect. The best moisturizers still up to trial trust as usually matters until data were being choosing the right moisturizing products beneficial for them. This paper review is to express and encouraging to people to know the physical quality of individual and psychological effects use of moisturizers having property as to hold-water capacity, auto-skin repair mechanically and influence them to the people who are suffered from skin related problems or those who cannot maintain their skin. Moisturizers usage with time rising demands as the world's wide population clients under different matures persons becoming more urbanized beautifying society. As the population ages and we turn into an urbanized makeover worldwide, the need of moisturizers use will increase.

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