

Functional Cosmeceuticals and Nano-Enabled Delivery Approaches in Dry Skin Management: A Mechanistic Review

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ABSTRACT

Dry skin(xerosis) is a prevalent skin disease defined by barrier impairment and decreased hydration in the stratum corneum, with increased trans-epidermal water loss (TEWL). Dry skin pathophysiology very complex, encompassing impaired intercellular lipid arrangement, disturbance of keratinocytes differentiation, loss of natural moisturizing factor (NMF), potentiated inflammatory reactions and elevated skin surface pH. Oxidative stress and barrier dysfunction are also exacerbated by various environmental condition, including ultraviolet light exposure, low humidity and irritants. Current therapies offer limited and short time relief, indicating the need for mechanism-driven and multi-functional therapies.

This review outlines the anatomical and physiological aspects of the skin, classification of skin types, and key mechanisms underlying dry skin. It highlights functional ingredients used in topical formulations, including barrier repair agents, humectants, emollients, occlusives, mild surfactants, antioxidants, and anti-inflammatory compounds. These agents act synergistically by restoring lipid bilayers, enhancing water-binding capacity, reducing TEWL, neutralizing reactive oxygen species, and modulating inflammatory pathways. The roles of synthetic, semi-synthetic, natural, and natural isolate compounds are also discussed, along with a mechanistic classification to guide targeted therapy. Overall, a multi-targeted formulation strategy is essential for effective dry skin management.

Keywords: Dry skin (xerosis); Stratum corneum; Transepidermal water loss (TEWL); Skin barrier function; Moisturizing agents; Cosmeceuticals

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INTRODUCTION

The Skin is a multifunctional organ that covers almost 20 square feet of the body. It occupies 15% of the total average adult body weight and acts as the first protective line and barrier with varied thickness. It is very adaptable and plays a distinct function across the human body. In anatomy, the skin is categorized into 3 main layers: dermis, epidermis and hypodermis. With these layers, the skin accomplishes six important function-Protection, thermal regulation and communication, Water storage, Neural relay network and Synthesis of Vitamin D [1]. Skin is a major water storage organ, normally in the hypodermis layer. It does have the capability to absorb some specifically lipophilic molecules. Due to changes in the blood flow, the position of hairs and the movement of those muscles that seep directly into the skin help to feel emotions like joy, fear and wrath[2].

Worldwide skin diseases ranked 4th among the leading causes of non-fatal disorder. Complains related to dry skin commonly increases in the general population[3]. As per the epidemiological data, standardized global survey conducted between January and April 2013, targeted individuals aged 16 years or older in 20 countries across five continents which almost cover 50 % of the population. Moreover, the study reported a global prevalence of Dry skin or AD of 9.6%[4]. Comparison with Indian population, the reported data mentioned that in India, the prevalence of the dry skin is around 42%, along with 28% of combination skin[3]. Among the general population dry skin is a highly prevalent condition. In clinical terms, dry skin causes scaly, rough and itchy skin, which is distinguished pathophysiologically by an agitated stratum corneum, impaired keratinocyte differentiation and dehydration [5]. Dry skin is an often condition caused by high

amount of moisture loss. The underlying reason of dry skin are very complicated and numerous caused by various environmental factors[6].

Treatment of these skin conditions with standard methods shows less therapeutic efficacy, systemic side effects, long treatment duration and reappearance of the condition. Since the skin covers a large area in the human body, that's why drug delivery through the skin shows top potential. It can be used for topical, dermal and TDDS[7]. Drug delivery to the skin is done by conventional formulation, which includes bioactive or cosmeceutical compounds in the form of lotions, gels, ointments and creams in the form of nano formulation or cream[8]. NewDay's, Moisturisers play essential role to maintain basic skin care regimen, and available marketed skin product that show promising results on dry skin. Occlusives agent, which protect the skin by forming hydrophobic layer. Humectant, which maximize the SC hydration by binding to water, or emollients, which can deeply connect the gaps between corneocytes and smooth the skin. Moreover, some product contain actives which bracing endogenous barrier repair [6]. But Bioactive and cosmeceutical compounds show effects on skin condition like dryness, hydration and elasticity[9]. Studies show that in dry skin, emollients containing one or more inactive ingredients (e.g. glycerol, urea, lactic acid, liquid paraffin) restore skin hydration. But newer compounds that contain active ingredients may increase the treatment option with better efficiency (e.g. almond oil, coconut oil, amino acid, Dexpanthenol, hyaluronic acid, vitamin E, glucose, glycerol, linolic acid, pyroglutamic acid)[10].

The etiology of dry skin condition is based on both the intrinsic and environmental factors. Due to the large surface area of skin, primary topical formulation of such as lotions, cream and moisturizer are the choice for the management of dry skin. These formulations act through occlusive and humectant by showing their action on various factors like TEWL, radiation therapy, temperature and humidity and detergents and irritants. An increasingly incorporates various ingredients to enhance hydration, restore barrier restoration and decrease the TEWL. The objective of this review is to critically assess various natural, natural isolate,

synthetic and semi-synthetic compounds based on their mechanistic role in improving barrier integrity, hydration and reducing inflammation responses in the management of dry skin.

ANATOMY AND PHYSIOLOGY OF THE SKIN

The skin comprises two layers: the upper layer (the epidermis) and the lower layer (the dermis), divided by an underlying membrane, - The Epidermis consists of 5 layers, the outermost layer called stratum corneum, which is only found in certain areas of the body. The skin has several layers, including the stratum granulosum, stratum spinosum and stratum Basale that consist of epidermal stem cells. One layer forming a strong physical barrier, which is mainly formed by the thick layer of dead cells (corneocytes) covered with a lipid layer called stratum corneum[11].The dermis layer is divided based on collagen content thickness into the Upper stratum papillae and the lower stratum reticulare, which contain thick and thin fibers of collagen[12].The third layer of skin that connects the dermis to the underlying fascia is called the hypodermis. Mostly, the hypodermis comprises vascular nerves, adipocytes, and adipose stromal cells (ASC). The Hypodermis layer is crucially responsible for maintaining thermoregulatory and mechanical qualities. It also regulates the top dermal and epidermal layer. This layer promotes fibroblast proliferation, wound healing, keratinocyte and most importantly, hair follicle cycling[13].Human skin contains both adaptive and innate immune cells, including natural killers (NKs), macrophages, mast cells, antigen-presenting cells (APCs), dermal dendritic cells and epidermal dendritic cells (EDCs). DCs, also called Migratory and interstitial DCs, among others, $\alpha\beta$ T cells, and B cells[14][15].

To serve as an immune response, sensation, or physical barrier (pain, touch, temperature, pressure perception carries out a variety of peculiar tasks enabled by the skin's special location and composition. Neuro-endocrine(closely linked to central stress axes), and homeostatic (by eliminating excess water, uric acid, urea and ammonia)[15].

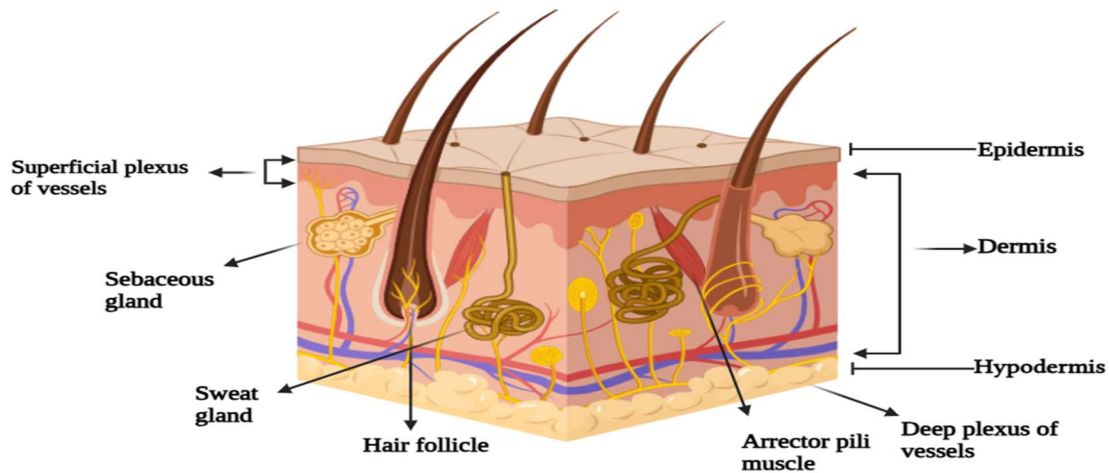


Figure 1: Anatomy of the Skin

The skin carries the inherent capacity to repair itself. It heals to reimpose its integrity, when an aggression breaches the cutaneous barrier. Sustain its function for a week in the event of moderate wounds[16].

2.2 Skin types

To classify skin into 16 kinds based on face traits, including dry or oily, resistant or sensitive, pigmented or non-pigmented, wrinkled or unwrinkled. In 2008, Leslie Baumann established an approach. Variation in sebum secretion ultimately causes skin type to change. Sebum secretion differs over the face

according to the different age groups. Sebum is mostly located on the forehead, cheeks, nose and chin. Oily and dry skin cause a major impact on the cosmeceutical market[17]. The basic average skin secretion for the entire face is 118.7-180.9 $\mu\text{g}/\text{cm}^2$, with the acidity level of 5.6-6 due to the acid available in secreted, keratin and sweat. The average sebum secretion rate for combo, oily and dry skin types is 204.6-235.4, 109.8-145.5 and 97.3-147.6 $\mu\text{g}/\text{cm}^2$, respectively[18]. (fig-2)

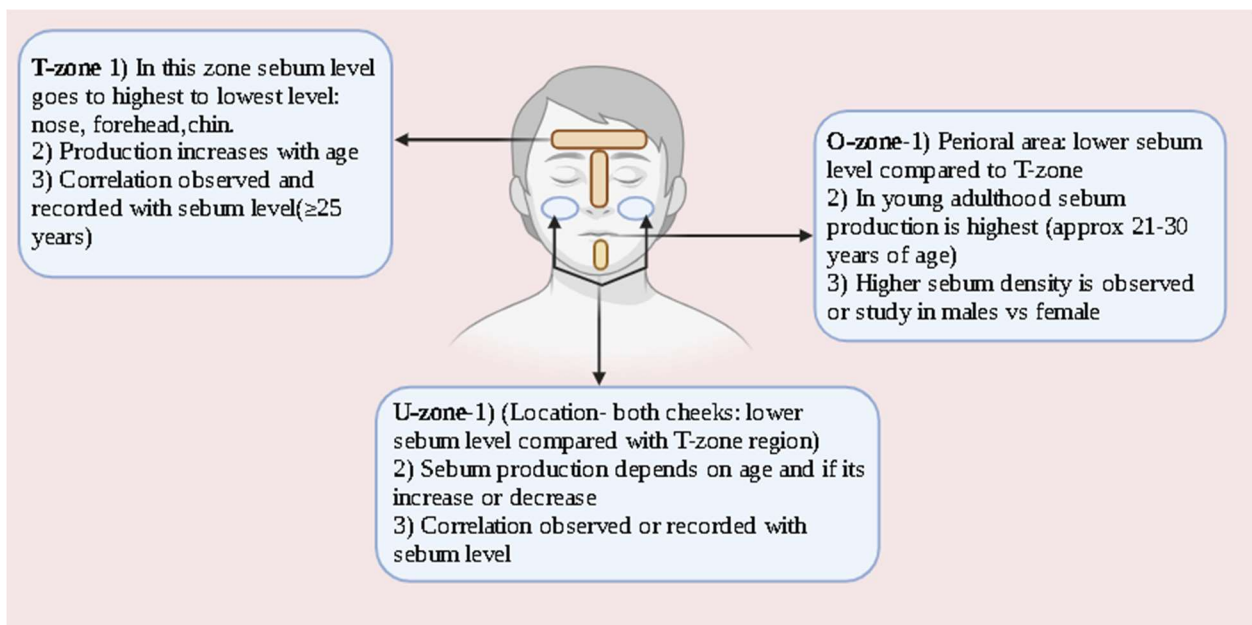


Figure 1 Sebum production at different facial region

The cosmetic material must be formulated according to the skin type. The product should provide hydration

and wipe out the excess sebum to expedite healthy skin [19].

Table 1: Reference value for the evaluation of facial skin types by sebum secretion measured with Sebumeter($\mu\text{g}/\text{cm}^2$)

Skin type	Whole Face (MFSE)	T-zone	U-zone
Dry	<25	<32	>13
Normal	25-82	32-92	13-68
Oily	>82	>98	>68

*MFSE= mean facial sebum excretion

2.3 Dry Skin

Due to a decreased stratum corneum water content, dry skin may have a thinner epidermis. Rather than that, water plays a crucial role in skin health. In the process of desquamation, skin cells are discharged into the environment in small amounts. In the absence of water, the cell-binding filament remains on the surface, does not disintegrate, resulting in visible cell blocks that resemble fish scales, further indicating the signs of dry skin. Due to dehydration, cracks, can form, providing a gateway for microorganisms, including pathogens[20]. The concentration of water in three different layers is the natural moisturising component. This type of factor

helps to maintain the mechanical qualities of the stratum corneum through its lipophilic nature[21].

2.4 Pathophysiology of Dry Skin

Majorly, filaggrin, a deficit is detected in dry skin, In the case of Dry skin, filaggrin mutation status is independent and sometimes in ichthyosis vulgaris, the shortage of filaggrin, which, is an important factor in the pathogenesis of the skin disorder. Due to the compromised skin barrier of dry skin, there is an increased PH, which is responsible for the entrance of allergens, irritants and germs into the skin, supporting the cyclic deterioration of skin homeostasis[22].(figure -3)

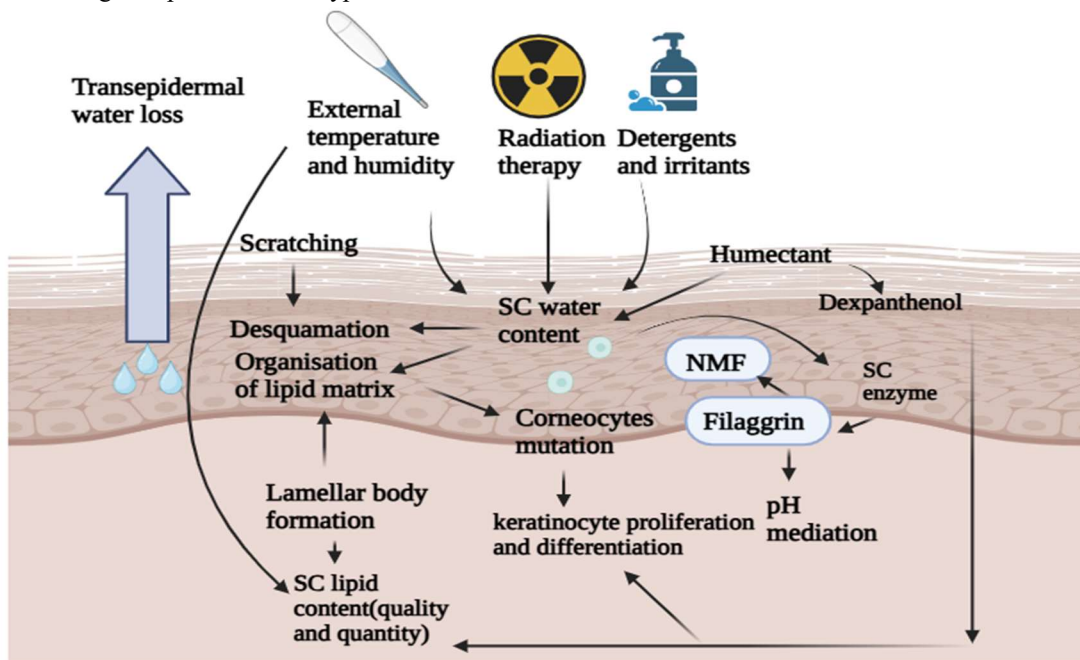


Figure 3: Pathophysiology of dry skin

*NMF- stands for Natural Moisturising Factor- it is a collection of water-soluble compounds (like amino acid, lactase, urea and salts).

*SC- Stratum corneum

2.5 Approaches to overcome factor causes dry skin

2.5.1 For transepidermal water loss

Replenish intercellular lipids (RIL) Fatty acids and ceramides can intensify lamellar organisation with

increased lipid pack density and therefore increase barrier strength [23]. Physiological lipids, which are applied topically, such as cholesterol, ceramides and free fatty acids, reduce TEWL, strengthening the skin

barrier by being incorporated into SC intercellular lipid matrix, normalising lipid ratio, and finally restoring bilayer organisation [24].

Forming occlusive layer (FOL) On the skin surface, occlusives form a hydrophobic layer, by lowering down TWEL and preventing from water evaporation. Occlusives are specially effective for combination or dry skin[25].

Restore lamellar structure of SC (RLS) The restoration of the SC lamellar structure implies to the re-establishment of structured lipid bilayer, which is essential for barrier function. Topical remedies comprises structured lipid system and ceramides have been shown the impact SC lipid organisation, promoting thicker lateral packing and larger lamellae in damaged or dry skin [23,26,27].

2.5.2 External temperature and humidity

Increased Natural moisturising factor (INMF) Natural moisturising factor is a combination of very-tiny water-soluble compound found on the upper layer of skin (SC). Soaking SC in water results in the extraction of water molecule of NMF, which further disrupts the molecular -level properties of SC and result in dry skin [28]. Furthermore, an escalated level of NMF content in the corneocytes increases the amount of water in the SC [29].

Enhanced water binding with corneocytes (EBC) Corneocyte components, along with NMF has retaining capabilities and water binding, which further allow corneocytes to absorb more than three times their weight in water. Moreover, the lack of these components causes dry skin and pathological diseases with excessive water loss [30].

Improve aquaporin-mediated hydration (IAH) The expression of aquaporin in keratinocytes mainly contributes to the barrier function and hydration of the SC. Aquaporins consist of 13 transmembrane protein channels that further regulate the homeostasis of the uncharged solute. The main role of aquaporin, especially aquaporin-3 promote water retention on the skin and skin hydration [31].

2.5.3 Radiation therapy-

Scavenge ROS (SROS) Primary cause of photodamage is UV, with several complications. ROS, as a signalling molecule, plays a crucial role in UV-induced photodamage, where high level of ROS is recorded. To overcome this, non-enzymatic antioxidants are used, including vitamin A, C and E and flavonoids. Moreover, by decomposing H₂O₂ and O₂, antioxidants help to lower the oxidative damage and ROS [32].

Inhibit UV- induced lipid peroxidation (IUVLP) Lipid Peroxidation is the major cause of the skin disorders or diseases caused by UV. The formation of lipid peroxidation was also noticed in UV-irradiated

epidermal keratinocytes without real continuing cell death[33]. When human keratinocytes are exposed to UV radiation, compound tocopherol provides photoprotection by elevating glutathione production, which further reduces ROS, lipid peroxidation and malondialdehyde levels [34].

Downregulate MMP and inflammatory pathway (DMMP) Fibroblast senescence can be caused by overexposure to UV radiation. Senescent fibroblast is distinguished by oxidative DNA damage and the breakage of double-strand DNA, as well as reduced extracellular matrix and an increase in matrix metalloproteinase (MMP) production. Flavonoids were reported to downregulate MMP-1 expression and the inflammatory pathway in UV- irradiated human dermal fibroblast[35].

2.5.4 Detergent and irritants

Anti-inflammatory and soothing action (AISA) Topical anti-inflammatory actives such as peptides and phytochemicals, quickly soothe the irritated skin by lowering the pro-inflammatory signalling, such as (e.g., NF- κ B), histamine and cytokine formation or sensory and immunological activation, which further reduces erythema, further increasing barrier healing and overall skin comfort[36].

Barrier reinforcement during cleansing (BRDC) When it's compared to harsh anionics, an advanced surfactant system, such as a biobased or polymeric surfactant, shows less barrier disruption. A mild cleanser has been dermatologically/clinically proven to maintain TEWL and other barrier parameters during routine use. Barrier reinforcement during cleansing refers to preventing SC integrity by minimizing surfactant- induced protein denaturation and lipid extraction[37][38].

2.6 Dermatological conditions in dry skin

There are various dermatological diseases which are associated with Dry skin, inflammatory skin conditions like Genodermatosis, Contact dermatitis, Infectious dermatosis and skin neoplasms[39].

2.6.1 Genodermatosis- it refers to a broad range of dermatoses caused by abnormalities in genetic structure, including mosaic and monogenic illnesses. Physio pathogenic factor such as epidermal and intraepidermal adhesion, DNA repair, and Cornification, disrupts numerous skin compartments. At birth or in early infancy, the clinical symptoms are visible, and the clinical course is progressive, with no spontaneous healing or remission[40].

2.6.2 Skin neoplasms- skin neoplasm is associated with a broad range of benign and malignant skin cancers. Neoplasm is characterised by the neoplastic growth of cells and tissue beneath the different skin layers; hence, they can result in substantial morbidity and ultimately death. UV radiation is the primary

factor to causes most forms of skin cancer, which include basal cell carcinoma, squamous cell carcinoma, and melanoma. With a variety of clinical characteristics, these tumours can appear and are frequently evaluated and diagnosed with biopsy and histological examination for the precise kind of treatment. This vast category of neoplasms may need a histopathological evaluation , and today’s advanced therapies, such as non-topical and topical treatments(anti-neoplastic injection), systemic medication like chemotherapy, etc[41].

2.6.3 Contact dermatitis- It is an inflammatory skin condition caused by irritating or allergic chemicals, tiny reactive allergens or metal ions that further modify protein structure to stimulate immunological responses through T-cells. Recorded symptoms are erythema, oedema, leaking, crusting and extreme

pruritus. At last, contact dermatitis is classified as Irritant Contact Dermatitis (ICD), allergic contact dermatitis (ACD), Immediate skin reaction, photoinduced CD and non-eczematous. CD can affect any age and gender[42].

2.6.4 Infectious dermatosis- infectious dermatoses cause erythematous desquamative rashes, which are a frequent dermatological issue in outpatient treatment. These types of disorder are frequently diagnosed by clinical-based, including morphology, distribution and laboratory tests. However, for some reasons, it is difficult to do a clinical diagnosis and needs histological sign confirmation due to overlapping signs. Although skin biopsy is typically safe, problems may occur with consequently, resulting delayed in management and diagnosis[43].

Table 2: Dermatological conditions associated with dry skin and their clinical characteristics

Condition	Etiology/Pathogenesis	Key Clinical Features	Diagnostic Approach	References
Genodermatosis	Genetic defects	Early onset, chronic	Clinical/genetic	[40]
Skin Neoplasms	UV damage	Tumors (BCC, SCC, melanoma)	Biopsy	[41]
Contact Dermatitis	Allergens/irritants	Itching, erythema	Patch test	[42]
Infectious Dermatitis	Microbial infection	Rash, scaling	Lab tests	[43]

MANAGEMENT OF DRY SKIN CONDITION

Compromised barrier function, major increment in the transepidermal water loss and reduced hydration are the main hallmarks of dry skin(xerosis), which is a very common dermatological disorder. Stratum corneum, known as the outermost layer of the skin, vital for protecting the skin from various environmental stressors and is hydrated. Furthermore, barrier disruption causes lipid depletion, inflammation and a reduction of natural moisturizing factor increasing sensitivity towards the invasion of the microbes and causing irritation. That’s why treatment for the dry skin requires a multitargeted approach that both tackles barrier restoration and hydration. For dry skin, various topical formulations are outlined for the incorporation of many ingredients that act as humectants, emollient agents, occlusives and barrier repair agents. Majorly, these categories show corresponding actions to improve hydration, restore skin homeostasis, reduce high inflammation and manage overall skin health. This segment provides an overview of these ingredients and their MOA of the management of dry skin.

3.1 Barrier Repair Agents

For the management and the treatment of the dry skin barrier repair agents play important role. Because the impairment of the stratum corneum barrier is the main pathological feature of dry skin. The stratum corneum act as a main protective barrier which protect the skin from surplus water loss and protect the skin from allergen, microbial invasion and environmental irritants [23,24]. Structurally, the stratum corneum is express by using brick- and-mortar model, in which intercellular lipid described as mortar and corneocytes as brick [26,27]. Intercellular lipids are arranged in lamellar structure which are mostly formed with cholesterol, ceramides and free fatty acids [23,44]. When there is barrier disturbance skin hydration decreases transepidermal water loss increases resulting rough, dry scaly and prone to high inflammation, irritation and redness [22,39]. In this case barrier repair agents shows their action by acting enhancing keratinocyte differentiation, restoring lipid composition, increasing the uptake of structural protein such as loricrin and filaggrin, reducing inflammation and ameliorate natural moisturizing factor production, thereby function of the

skin barrier and restoring the integrity [24,31,45]. In dermatological formulation most of the barrier repair agents are synthetic, because of its predictable activity and best targeted molecular mechanistic insight. Best example is **Niacinamide (nicotinamide)** reflecting as vitamin B3, in keratinocytes niacinamide restoring ceramide synthesis, which is helpful for the restoration of lipid matrix of the stratum corneum. It also increases the production of free fatty acids and cholesterol, which are essential components of the skin barrier [46-48]. In addition, niacinamide exhibits anti-inflammatory properties by inhibiting inflammatory mediators and reducing erythema and irritation [49]. It also improves keratinocyte differentiation and increases the expression of barrier proteins, thereby reducing transepidermal water loss and improving skin hydration and elasticity [49,50].

Dexpanthenol, a provitamin of pantothenic acid (vitamin B5), contributes to barrier repair through its role in coenzyme A synthesis, which is involved in lipid metabolism and synthesis of fatty acids. It enhances fibroblast proliferation, promotes epidermal regeneration, accelerates wound healing, and improves hydration by increasing water binding in the stratum corneum [51,52]. Dexpanthenol also exhibits anti-inflammatory effects and improves skin elasticity and softness [53].

Urea is another important synthetic barrier repair agent that functions by increasing water-binding capacity and enhancing keratinocyte differentiation. It also increases the expression of genes involved in lipid synthesis and barrier formation while improving aquaporin expression, which enhances water transport within the epidermis. At lower concentrations, urea acts primarily as a humectant and barrier repair agent, whereas at higher concentrations it acts as a keratolytic agent that removes excess keratin and improves skin smoothness and permeability [54,55].

Semi-synthetic barrier repair agents are derived from natural lipids and compounds but are chemically modified to improve stability and formulation compatibility. **Ceramide NP** is one of the most important semi-synthetic barrier repair agents because ceramides constitute a major portion of intercellular lipids in the stratum corneum. Ceramide NP integrates into the lipid bilayers of the stratum corneum, restoring the lamellar lipid structure and improving barrier

integrity. It reduces transepidermal water loss, improves hydration, and enhances keratinocyte differentiation [24,26,44].

Ceramide NP also acts on peroxisome proliferator-activated receptor (PPARs) that mostly controlled epidermal differentiation and lipid synthesis, resulting a good long-lasting repair of skin barrier [27,56].

Stearic acid, is a long chain fatty acid, which facilitates barrier repair by replacing various depleted free fatty acids in the lipid matrix of the stratum corneum. Main functions of the steric acid to enhance or improve membrane fluidity, internal cohesion of lamellar lipid system, lipid structuring and reduces transepidermal water loss while enhancing skin hydration. Additionally, it involves in signalling pathway related to epidermal differentiation and inflammation [57].

Sucralfate is a complex derivative of aluminium hydroxide and sucrose sulphate, mainly provide protective covering over abrasions, also shows the better healing capabilities on the wound. It initiates the production of growth factor. Moreover, they show increased hydration, with anti-irritant and anti-inflammatory effect by proliferation of keratinocytes [58].

Phytosterol combined with octyldodecyl lauroyl glutamate is a ceramide which is lipoamino derivate that relate or mimics the skin's natural lipids. Which further allow is to integrate into lipid matrix of the stratum corneum that reduces transepidermal water loss, improve lipid structuring and enhanced skin hydration. Additionally, this compound reduce irritation and improve skin smoothness. Lastly, it is beneficial in the formulation used for sensitive and dry skin [59].

Lipid rich and plant oil natural substances that restore the skin's lipid barrier also capable as natural barrier repair agents, as they are categorised as abundant fatty acids that repair the skin's lipid barrier and stimulate ceramide synthesis [60,61].

By modulating aquaporin-3 and enhancing the expression of filaggrin **Coconut oil** also play a major role in improving the skin barrier, which further decrease transepidermal water loss and improves hydration. Moreover, it also acts anti-microbial and anti-inflammatory agent [62,63].

Olive oil majorly formed by linolic acid, oleic acid and some phenolic antioxidant that restore lipid barrier structure, provide anti-oxidant protection with better corneocyte regeneration [64].

Almond oil, rich in oleic acid, linoleic acid, and vitamin E, improves lipid barrier function, reduces transepidermal water loss, and enhances skin hydration and elasticity [65,66].

Avocado oil contains essential fatty acids, phytosterols, and vitamins that promote collagen synthesis, improve skin regeneration, and restore the lipid barrier, thereby improving hydration and skin softness [67,68].

Natural isolate barrier repair agents are purified lipid and bioactive compounds that directly influence barrier repair mechanisms at the molecular level.

Linoleic acid plays a crucial role in ceramide synthesis and epidermal barrier formation, thereby improving lipid barrier integrity and reducing transepidermal water loss [69].

β -sitosterol enhances the expression of barrier proteins such as filaggrin, loricrin, and aquaporin-3, thereby improving skin barrier integrity and hydration [70,71].

Glycyrrhizin acid improves barrier repair through its anti-inflammatory and anti-allergic properties while also improving hydration and reducing irritation in sensitive and atopic skin [72-74].

Resveratrol contributes to barrier repair by upregulating barrier proteins and reducing inflammatory cytokines, while also providing antioxidant protection against oxidative stress that damages the lipid barrier [75,76].

3.2 Humectants

Humectants represent one of the most essential classes of moisturizing agents used in the management of dry skin, primarily due to their ability to attract and retain water within the stratum corneum. The hydration level of the stratum corneum is a critical determinant of skin health, as reduced water content leads to dryness, scaling, roughness, and impaired barrier function [30,39]. Generally, in normal condition intercellular lipids, environmental humidity and temperature and lastly natural moisture factor (NMF) which maintain normal level of water in stratum corneum between 10-20% [28,29]. Xerosis, psoriasis, aging and atopic dermatitis are the dry skin conditions caused by depleted NMF, compromisation of hydration and increase in transepidermal water loss (TWEL) [22,31].

Humectant are vital for improving hydration and moisture. Mostly worked in the presence of hydrophilic functional group such as amide, hydroxyl and carboxyl group eligible humectant to attract and bind with water which further leads to improve or enhance skin softness, elasticity and strengthens the skin barrier function [77,45].

The effectiveness of synthetic humectant, along with their availability and stability, has made them popular in dermatological and cosmeceutical product.

Likely one of the most of widespread humectant is **glycerine** which is also known as glycerol. Glycerine shows their action because of their three-hydroxyl group that allow it to form various hydrogen bond with water molecules. Which results moisture attraction from the environment into the stratum corneum [78]. Moreover, glycerine increase the functionality and various expression of aquaporins- notably, aquaporin (AQP3) plays a major responsibility for the transport of water and glycerol in keratinocytes and ensure intracellular hydration. At last, by regulating major enzymes activity in the stratum corneum, which ensure proper prevention, desquamation and scaling, while indirectly maintaining and stabilize lipid bilayers and transepidermal water loss [38,79].

Another artificial humectant is **propylene glycol** which contain hygroscopic features meaning it is also proficient of attracting water into the stratum corneum. Propylene glycol is capable of destabilize the intercellular lipid structure, thus improving penetration of active compounds into the skin [80]. It also increases the water binding capacity in corneocyte, soften keratin and as well as exhibiting mild antimicrobial feature [81].

Other similar compound like **butylene glycol** which acts as both solvent and humectant. In fact, it keeps the hydration level of the stratum corneum well stable and increase the spreadability of the various topical product [77]. Also, butylene glycol prevents evaporation of water from the skin and make sticky free formulation without making the distortion in hydration level [82].

As opposed to natural humectants, semi-synthetic humectants have the same natural origin, but they specially modified for ensuring the enhanced stability and better absorption rate throughout the skin. The most popular humectant with the most water retention ability is **Hyaluronic acid**. Additionally, it holds up to

1000 times more water than its weight, with its highly hydrophilic nature and polymer-based structure with repeated disaccharides units [83]. By creating a film on upper layer of the epidermis hyaluronic acid preventing further evaporation from the skin. Moreover, this acid improves the hydration of extracellular matrix, stimulates cell regeneration, increase skin elasticity and also shows anti-inflammatory effect with wound healing properties [84].

Sodium lactate, a salt of lactic acid and one of the main components of natural moisturizing factor (NMF), which plays a vital role in hydration since it binds and attract water to the stratum corneum. This compound further helpful in maintaining the acidic skin pH, Ph level is important in the process of enzyme activity during the process of lipid formation and desquamation. Moreover, sodium lactate maintaining the decent lipid barrier integrity and good skin hydration, by swelling the corneocytes making them more flexible [85,86].

Glyceryl glucoside, another semi-synthetic humectant which stimulates the formation of aquaporin-3 and further promotes the process of water transportation through epidermis. It increases the cellular hydration as an additional component on natural moisturizing factor, and capable to increase the hydration of stratum corneum. This substance also boosts or enhances cellular metabolism and provides the vitality to dry or aging skin conditions [87,88].

Natural humectants come from biological and botanical origins which is widely used in cosmeceuticals because their ability to blend well and show multiple action in single formulation. **Glycerine** which is obtain from natural sources works much similar like synthetic glycerine which hold or attract moisture with in stratum corneum layer. It also supports barrier repair by stabilizing lipid organization and reducing dryness and scaling [38,78,79].

Royal jelly, a secretion rich in proteins, amino acids, lipids, vitamins, and minerals, acts as a natural humectant by providing amino acids that function as natural moisturizing factor (NMF) components. It enhances water retention in the epidermis, promotes keratinocyte proliferation and regeneration, and improves skin elasticity and hydration. In addition, its antioxidant and anti-aging properties contribute to overall skin health [89,90].

Aloe vera is another important natural humectant containing polysaccharides that bind water and form a protective hydrating film on the skin surface. It improves water retention in the stratum corneum, enhances fibroblast activity, stimulates collagen synthesis, and provides anti-inflammatory and soothing effects. Aloe vera also promotes wound healing and skin regeneration while reducing irritation and improving barrier function [91,92].

Natural isolate humectants are purified compounds obtained from natural sources that specifically mimic or enhance the function of natural moisturizing factor.

Lactic acid, an alpha-hydroxy acid, acts as both a humectant and mild keratolytic agent. It increases water content in the stratum corneum by attracting and binding water while also enhancing ceramide synthesis and improving lipid barrier function. Additionally, lactic acid promotes desquamation by breaking down corneocyte bonds, thereby improving skin smoothness and texture. It also maintains the acidic pH necessary for optimal enzymatic activity in the skin [93,94].

β -sitosterol, a plant sterol, contributes to hydration by stimulating hyaluronic acid synthesis and increasing the expression of barrier proteins such as filaggrin, loricrin, and aquaporin-3. This enhances water retention, improves barrier integrity, and reduces inflammation [70,71].

Glycyrrhizin acid, derived from licorice root, improves hydration by increasing water retention in the epidermis and enhancing the permeability of active compounds in topical formulations. While supporting or manage the barrier repair and skin soothing effect, it also exhibits anti-allergic and anti-inflammatory effect majorly used in sensitive and atopic dermatitis [72-74].

3.3 Occlusive and Emollient Agents

Emollients and occlusives play a significant role in managing dry skin by increases the softness, flexibility and skin hydration by reducing TEWL. On the other side, humectant only bind or attract the water molecules in the stratum corneum, whereas occlusive act by forming hydrophobic barrier, which result in reduced water evaporation and thus preserves moisture [95, 96]. However, emollients work by filling inter-cellular spaces between corneocytes, which further reducing roughness, provide smoothing effect on skin surface and improving the elasticity [25,31]. Xerosis, eczema, psoriasis and dermatitis are the condition

caused by dry skin associated with aging reason is impaired lipid matrix which further caused increased TEWL irritation and scaling [22,39]. These all compounds managing or restoring the lipid layer and strengthening the skin barrier effect [45].

Synthetically produced occlusive agents are oftenly used in vast range of dermatological products because of their stability and barrier forming ability. **Mineral oil** functions similarly to petrolatum but provides better spreadability and a lighter texture. It forms a thin hydrophobic film that reduces water loss while improving skin softness and lubrication. Mineral oil also enhances the smoothness of the skin surface by filling micro fissures between corneocytes, thereby reducing roughness and improving tactile properties [78].

Petrolatum termed as best occlusive compound, because they lower down transepidermal water loss by up to 98%. This compound form semi-occlusive and hydrophobic layer on surface of the skin, which further preventing evaporation of moisture or hydration, improved swelling of corneocytes and better barrier repair. Moreover, petrolatum assists lipid reorganization and show healing effect on damaged skin or within the stratum corneum [38,97].

Dimethicone, a silicone-based compound, differs from traditional occlusives by forming a breathable, flexible barrier on the skin surface. Its mechanism involves the formation of a semi-permeable film that prevents excessive water loss while still allowing gas exchange. Dimethicone also improves skin texture by filling irregularities in the skin surface, reducing roughness, and providing a silky, non-greasy feel. Additionally, it protects the skin from environmental irritants and enhances the aesthetic appeal of topical formulations [78].

Semi-synthetic occlusive and emollient agents are derived from natural compounds but are chemically modified to enhance their performance and stability. The well-known fatty acid known as **Cetearyl alcohol** is a surfactant that majorly act as an emulsifier and emollient. Cetearyl alcohol works on the mechanism in which formation of lipid layer on the skin to reduce high water loss, resulting increased hydration. Additionally, it fills gaps between the corneocytes, making the skin feels more softer and smoother. By lowering down the surface tension it helps to stabilize the emulsion, which further improve formulation spreadability and consistency [98,99].

Isopropyl myristate, a well-known fatty acid ester, an emollient but used as penetration enhancer. This compound comes with excellent spreadability on the skin surface, form a thin lipid layer that improve skin lubricity and reduce transepidermal water loss. Isopropyl myristate is having low viscosity which allow it to penetrate easily throughout the skin outermost layer, by disrupting the lipid packaging isopropyl myristate increases the absorption of active ingredients. Additionally, it comes with non-greasy feel, making it eligible for various cosmetic formulation [100].

Sorbitan olivate, is a naturally sourced emulsifier, act as both emollient and occlusive agent. It helps in forming a protective layer over the skin surface and improve its hydration capacity with maintained moisture level. Moreover, sorbitan olivate makes the emulsion more stabilize with even allocation of active ingredient. Its main function is to improve lipid ordering in the stratum corneum layer [101,102].

Emollient and occlusive also derived naturally from plants sources such as waxes, oil and butter and are mainly used because of their multiutility and biocompatibility feature. For example, **Beeswax** primarily acts as semi-occlusive agent which reduces transepidermal loss bounded moisture exchange by forming defensive film over the skin surface. Although, it provides anti-inflammatory and anti-microbial properties and provide best structural integrity to formulation [95,103].

Plant-based wax like **Carnauba wax** performs same function through the formation of hard protective layer that helps skin protect against external environment and prevent moisture loss [104,105].

Natural oils like **olive oil, coconut oil, argan oil, jojoba oil, avocado oil, shea butter and almond oil** act as best emollients, as they replace lost lipids by entering intercellular space of stratum corneum. This type of oils contains huge amount of fatty acid, which permeate the lipid matrix easily, enhance barrier activity and decreasing transepidermal loss. An example is coconut oil which has medium-chain fatty acid that further promotes lipid organization with antimicrobial properties.

There is oil which is a rich source of phenolic compounds and oleic acid called **olive oil**, which enhances skin regeneration and flexibility.

Argan oil offers best anti-oxidant effect with enhanced elasticity and jojoba oil also has similar sebum structure and balance out hydration level and excessive dryness [60,61].

Additional oils such as **almond oil** and **shea butter** alleviate inflammation, make the skin soft and by creating protective lipid layer these oils improve hydration [62,63,64,65,66,67,106].

Natural isolate emollients and occlusive are majorly purified lipid compounds which play a direct role in hydration and barrier properties. **Squalene**, which is a natural ingredient of the human sebum that's why it having good occlusive properties which create a light lipid layer on skin surface, which preserve skin flexibility and decreases transepidermal water loss. Moreover, it also possesses anti-oxidant effect resulting prevention from oxidative damage of skin lipids [107,108,109].

Palmitic acid contains saturated fatty acids helps in occluding the skin by forming a lipid layer which further minimize water loss and maintain hydration or enhance skin elasticity and smoothness. Palmitic acid also involves in structural integrity of lipid barrier [110,111].

Linoleic acid which is an essential fatty acid responsible for better epidermal barrier maintenance and ceramide synthesis. By enhances the lipid matrix linoleic acid enhances hydration and lowering down transepidermal water loss, with anti-inflammatory properties [69,112].

Oleic acid, which act as a penetration enhancer and emollient by breaking down stratum corneum lipid packing, making the skin soft and allowing the any active ingredients to permeate the skin. By forming the lipid film over skin surface oleic acid improves skin elasticity and decrease water loss [69].

3.4 Surfactants and Mild Cleansing Agents

Surfactant and mild cleansing agents are important in dry skin management, since inadequate cleansing resulting damaging the skin barrier and aggravate the dryness. Surfactant mainly used to wash the skin surface like excess sebum, sweat, dirt and various cosmetic residue and microorganism [37,80]. Nevertheless, severe surfactant may harm natural moisturizing factor and intercellular lipid from the stratum corneum. Hence it is responsible for rise in transepidermal water loss (TEWL), disruption in

barrier and skin irritation [30,31]. That why mild surfactants are thus desirably used on delicate or dry skin, since they wash the skin without causing an imbalance on the lipid barrier [59,113]. Mild cleansing agents are designed to maintain skin hydration, preserve barrier integrity, and reduce irritation while still providing effective cleansing.

Surfactants function by reducing surface tension between oil and water, allowing dirt and oil to be emulsified and removed from the skin surface. They contain both hydrophilic and lipophilic groups, which enable them to interact with water and lipids simultaneously. When applied to the skin, surfactants form micelles that surround dirt, oil, and impurities, allowing them to be washed away with water [37,80]. Mild surfactants are specifically designed to have larger micelle structures, lower penetration into the stratum corneum, and reduced interaction with skin proteins and lipids, thereby minimizing irritation and barrier damage [113,114].

Synthetic mild surfactants such as sodium lauryl sulphate derivatives and amphoteric surfactants are sometimes used in dermatological cleansers, but modern formulations increasingly use non-ionic and amino acid-based surfactants due to their better skin compatibility. These surfactants remove the excess dirt but preserve lipid content and are also capable of keeping the skin hydrated [37,38]. The non-ionic surfactant is less irritating compare to other surfactant because of their non-ionisable nature in water, that why interaction with lipids and skin protein are less aggressive. Whereas amino acid-based surfactant is closely related to natural skin and so are used in dry and sensitive skin cleanser [113,114].

Amino acid and mild sugar based semi-synthetic based surfactant are very popular in dry and sensitive skin formulation. One of the best examples is **Decyl glucoside** is a non-ionic surfactant mainly made out of fatty alcohols and glucose and known to be very skin friendly and mild. Its main mechanism is to create micelles which trap most of the oil and dirt without interacting strongly with lipids and protein. It is a non-ionic, therefore it does not disrupt the lipid barrier and does not denature protein in keratinocytes. Additionally, decyl glucoside decreases irritation and keep the skin hydrated and can be used in dry and

sensitive skin formulation, facial cleanser and baby preparation [115,116].

Lauryl glucoside is yet another most usable non-ionic surfactant, which is derivative of lauryl alcohol and glucose. On the basis of functionality both lauryl and decyl glucoside are same. But this compound offers powerful cleansing and foaming. It works by emulsifying oils, remove impurities through micelles formation and preserve lipid barrier integrity. By forming stable foam lauryl glucoside enhances sensory attributes of cleanser without being irritant or remain mild skin. This compound also aids in maintaining moisture balance in the skin by avoiding excessive loss of natural lipids from the skin [113,117].

By using amino acid derivative of glutamic acid and coconut fatty acid **sodium cocoyl glutamate** is formed. Known as least harsh surfactant in cosmeceutical and dermatological preparation. By interacting with skin lipid and protein this compound clean gently by forming micelles. It is very biocompatible with skin because of the amino acid profile that ensure the maintained skin natural pH. It also creates a very thin conditioning film on the skin while washing, which lower down skin dryness and enhance skin softness. Additionally, sodium cocoyl glutamate is less irritating and useful in preserving the barrier properties [114].

Nowadays, natural surfactant is found in the form of surfactant as well and mainly useful in herbal and natural skincare preparation. **Saponins** derived from natural resources lower the surface tension and create foam to remove oil and dirt. Saponins also mild and clean the skin, relatively milder than synthetic surfactant and frequently used in herbal cleansing preparation [118].

Lecithin is a type of phospholipid that is a derivative of egg and soy, serves as a mild emulsifier and surfactant. It works through the creation of lipid bilayer structure which further emulsify the oil and repair the skin and maintain the skin hydration. Because lecithin is structurally similar to skin lipids, it helps maintain barrier integrity while cleansing and improves skin softness and moisture retention [119].

Natural isolate surfactants include purified phospholipids and amino acid-based surfactants that are highly compatible with the skin barrier. These surfactants cleanse the skin without disrupting the lipid matrix and often provide additional moisturizing and

barrier-repair benefits. They also reduce irritation and improve skin feel after cleansing by forming a protective film over the skin surface [99,105]. Because phospholipids and amino acid-based surfactants are structurally similar to biological membrane components and natural moisturizing factor constituents, they exhibit high biocompatibility and help maintain barrier integrity while cleansing [61].

3.5 Antioxidants and Skin Protective Agents

Antioxidants and skin protective agents play an important role in the management of dry skin because oxidative stress is one of the major factors responsible for skin barrier damage, inflammation, premature aging, and loss of skin hydration. The skin is constantly exposed to environmental stressors such as ultraviolet radiation, pollution, chemicals, and microorganisms, which generate reactive oxygen species (ROS) such as superoxide radicals, hydroxyl radicals, and hydrogen peroxide. These reactive oxygen species damage lipids, proteins, and DNA in skin cells, leading to lipid peroxidation, collagen degradation, inflammation, and disruption of the skin barrier [37,120]. Damage to intercellular lipids and structural proteins results in increased transepidermal water loss and decreased skin hydration [30, 31]. Antioxidants help prevent this damage by neutralizing free radicals, protecting lipids and proteins, reducing inflammation, and improving barrier function and skin hydration [120].

Synthetic antioxidants are commonly used in dermatological and cosmetic formulations to protect the skin from oxidative stress and environmental damage. **Vitamin E (tocotrienols)** is a lipid soluble type antioxidant which prevent intercellular lipids and cell membrane from lipid peroxidation by donating some hydrogen atom to free radicals and stabilizing them. This provides a relief from oxidative stress on cholesterol, fatty acid and ceramides in the stratum corneum lipid matrix as a result minimize transepidermal water loss with preserved barrier. Vitamin E also has noticeable effect on skin hydration, elasticity with best anti-inflammatory effects [121-123].

Vitamin C (ascorbic acid) is an antioxidant rich (water soluble) compound that counter the effect of reactive oxygen species in the aqueous surrounding of the skin. Since it is a major cofactor to lysine and proline hydroxylase which is responsible for collagen

formation thus enhancing skin elasticity and structure [124]. Furthermore, vitamin C is responsible for vitamin E synthesis, which has been oxidized thus offering anti-oxidant synergistic defence. Vitamin C also lower down hyperpigmentation by suppressing melanin production in the body. And improve texture of the skin with enhancement in brightness [125].

Semi-synthetic anti-oxidant derived out of natural phenolic compounds but according to the skin type or condition they are modified or stabilized to increase skin penetration and formulation stability. **Ferulic acid** is a type of phenolic antioxidant that commonly used in many cosmeceutical preparation reasons behind is high free radical scavenging power. Its mechanism based on causing interference with reactive oxygen species and lipid peroxidation with in the skin barrier [126]. This compound also preserves vitamin E and C by boosting their photoprotective properties and antioxidant properties. Moreover, it triggers the Nrf2 antioxidant pathway which drastically enhances the expression of intrinsic antioxidant enzyme like catalase and superoxide dismutase. Ferulic acid preserve hydration and barrier integrity by inherent protective mechanism of the skin major oxidative stress [127,128].

Another example of semi-synthetic antioxidant which is having skin lightening and antioxidant effect is **kojic acid**. This compound act by chelation of metal ions like copper and iron, which play a part in making free radicals. By binding with these metals kojic acid decreases oxidative stress and preventing damage of skin cells. It also blocks tyrosinase enzyme responsible for the production of melanin, hence there is low hyperpigmentation and enhanced skin colour. Additionally, this compound shows anti-inflammatory and anti-oxidant response which helps to protect the skin [129,130].

Natural antioxidants are derived from plant extracts, oils, and natural products that contain polyphenols, flavonoids, carotenoids, and vitamins. **Green tea extract** contains catechins such as epigallocatechin gallate (EGCG), which neutralize free radicals and reduce oxidative stress [131]. These compounds also reduce inflammation by inhibiting inflammatory cytokines and enzymes such as cyclooxygenase and lipoxygenase. Green tea polyphenols also protect collagen and elastin from degradation and improve skin elasticity and hydration [132].

Aloe vera contains vitamins, flavonoids, and polysaccharides that provide antioxidant and anti-inflammatory effects while also improving hydration and wound healing [91,92].

Turmeric contains **curcumin**, a powerful antioxidant and anti-inflammatory compound that neutralizes reactive oxygen species and reduces inflammation by inhibiting NF- κ B signalling pathways [133]. Curcumin also improves wound healing, collagen synthesis, and barrier repair, thereby improving skin hydration and elasticity [134].

Natural isolate antioxidants are purified bioactive compounds obtained from plants and natural sources that provide targeted antioxidant activity.

Resveratrol, a polyphenol found in grapes and berries, exhibits strong antioxidant activity by scavenging free radicals and activating cellular protective pathways that protect cells from oxidative stress and aging. It also improves barrier function by reducing inflammation and protecting intercellular lipids from oxidation [135].

Quercetin, a flavonoid antioxidant, neutralizes reactive oxygen species and inflammatory mediators, thereby protecting the skin barrier and reducing irritation [136,137].

Coenzyme Q10 (ubiquinone) is an inherent antioxidant available on skin surface that naturalizes free radicals and provide mitochondrial energy production generated through cellular metabolism. Thus, compound enhances collagen synthesis, which further reduces skin wrinkles and improve skin elasticity with maintained hydration by defending cellular membrane from oxidative damage [138].

3.6 Anti-inflammatory and Skin Soothing Agents

The role of skin calming and anti-inflammatory agent in the management of dry skin is generally significant. Because dry skin correlated with typical irritation, inflammation, redness and barrier damage of the skin [2,13]. When there is a loss of skin barrier allergens and external irritants more readily enters the skin which further causes inflammatory reactions. This result in the discharge of inflammatory mediators like prostaglandins, histamine and cytokines causes itching, redness and irritation [2,13,27,37]. Moreover, chronic inflammation disturbs the skin barrier, which elevates the level of transepidermal water loss and increased dryness. Thus, calming and anti-inflammatory substances are the major compound which target at the

atopic, sensitive and dry skin. Also, these compounds enhance skin hydration, enhance barrier healing and diminish inflammation [2,13,25,37].

Moreover, synthetic anti-inflammatory compound used in many dermatological preparations include that compound which enhance skin barrier and inhibit inflammatory mediators. Currently, **Allantoin** is a basic skin rejuvenating agent that helps in regeneration of the skin and healing of wounds. This compound act by stimulating the growth of keratinocytes and repair the broken skin barrier by regenerate the epithelial cell. Additionally, it decreases the redness, irritation and elevates the level of water level in extracellular matrix which enhances the skin softness and state of hydration level [139,140].

Provitamin B5 or panthenol is an anti-inflammatory humectant which decreases the level of inflammation by enhancing the ability of the skin barrier and lowering down the irritation by increasing the moisture content on the skin layer. Panthenol mainly enhancing the growth of fibroblast proliferation, skin hydration, elasticity, epithelization and wound healing. Additionally, it minimises irritation and itching that mainly caused dry skin condition [51-53].

Anti-inflammatory semi-synthetic compounds are derived naturally but sometime they are modified to enhance their performance and stability in various formulations. **α -Bisabolol** is the one of the compounds derived from chamomile which is a skin calming and anti-inflammatory agent. its acts by blocking prostaglandins and inflammatory cytokines and thus provide a positive effect on redness or irritation. Moreover, this compound increase penetration and promotes healing ideally used for formulation used to manage irritated and sensitive skin without causing any side effects [141].

From *Centella asiatica* **madecassoside** is extracted, which is another semi-synthetic ingredient used in many cosmeceutical formulations. Its main action is to stimulate collagen formation, decrease inflammation, accelerate wound healing and stimulate fibroblast

activity which further enhances skin regeneration and making it suitable for damaged and dry skin [142].

Natural soothing agents are more commonly used in natural and herbal skin care products or formulation due to their versatility and safety. In moderns' days, **Aloe vera** is a most commonly used natural soothing agents. It is having moisturizing, anti-inflammatory and best wound healing properties because aloe vera is having vitamins, polysaccharides, amino acids ad enzymes. Moreover, aloe vera exerts an anti-inflammatory effect by disrupt inflammatory mediators and has soothing and cooling effect on the layer of skin [91,92].

Oat extract, especially colloidal oatmeal, is an another anti-inflammatory and skin protector. Oat extract having avenanthramides that decrease inflammation, irritation, itch and enhance barrier function and maintain the hydration level of the skin [143].

Chamomile extract has flavonoids and essentials with anti-oxidant, anti-inflammatory and calming properties making them ideal for dry and sensitive skin [144].

Plant derived anti-inflammatory compound contains many purified bioactive substance that specially target inflammatory events. **Glycyrrhetic acid and glycyrrhizin** is a compound found in licorice root that have potent anti-inflammatory properties due to their ability to suppress cytokines and inflammatory enzymes. They also restore hydration, barrier function and lower down irritation, itching and redness [72-74].

Another most popular natural compound **Curcumin** derived from turmeric, it is anti-inflammatory compound that block NF-kB pathway and inflammatory enzyme, thus decrease oxidative stress and inflammation. This compound also show barrier enhancing and wound healing properties [133,134].

A naturally derived dicarboxylic acid named as **azelaic acid** has anti-microbial, anti-inflammatory and keratoregulatory activity, making it best suitable compound for inflammatory skin condition with irritation, dryness and enhances skin hydration shows in recent studies [145].

Table 3: functional ingredients in dry skin therapy: representative compounds, mechanisms, and main function.

Category	Representative Compounds	Mechanism of Action	Primary Function(s)	References
Barrier Repair Agents	Niacinamide, Dexpanthenol, Urea, Ceramide NP, Linoleic acid, β -sitosterol	Stimulate ceramide/lipid synthesis; enhance keratinocyte differentiation; increase barrier proteins and NMF	Restore lipid matrix, \downarrow TEWL, improve barrier integrity	[24,26,27,44,46-50,51-53,54,55,56,57,69,70,71]
Humectants	Glycerine, Propylene glycol, Hyaluronic acid, Sodium lactate, Lactic acid	Bind water via hydrophilic groups; enhance AQP3 expression; increase SC hydration	Improve hydration, elasticity, barrier support	[78,79,80,81,82,83,84,85,86,93,94]
Occlusive & Emollients	Petrolatum, Mineral oil, Dimethicone, Plant oils, Shea butter, Squalene, sorbitan olivate	Form hydrophobic barrier; fill intercellular spaces; replenish lipids	\downarrow TEWL, improve softness and flexibility	[38,78,97,98,99,100,101,102,103,107-109]
Mild Surfactants	Decyl glucoside, Lauryl glucoside, Sodium cocoyl glutamate, Lecithin, saponins	Gentle micelle formation; minimal disruption of lipids/proteins	Cleansing while preserving barrier	[113,114,115,116,117,118,119]
Antioxidants	Vitamin C, Vitamin E, Ferulic acid, Resveratrol, Green tea extract, CoQ10	Neutralize ROS; prevent lipid peroxidation; activate antioxidant pathways	Protect barrier, reduce oxidative stress	[121-123,124,125,126-128,131,132,135,138]
Anti-inflammatory & Soothing Agents	Allantoin, Panthenol, α -Bisabolol, Aloe vera, madecassoside Oat extract, Curcumin, Glycyrrhizin	Inhibit cytokines/NF- κ B; promote healing and regeneration	Reduce irritation, support barrier repair	[51-53,139,140,141,142,143,72-74,133,134]

DISCUSSION

The present review elucidates the mechanistic insights explaining the multifactorial pathophysiology behind the dry skin condition. The study integrates diverse category of active compounds such as barrier repair agents, humectants, occlusive and emollient agents, mild surfactants, antioxidants, and anti-inflammatory agents targeting the multiple physiological pathways underlying dry skin condition.

Barrier repair agents such as ceramides, niacinamide, and linoleic acid acts by restoring the lipids composition and promoting keratinocyte differentiation resulting in enhanced structural integrity of the stratum corneum. Humectants including glycerine and hyaluronic acid improve water retention through hygroscopic mechanisms and modulation of aquaporin channels, thereby enhancing hydration at both anterior and deeper epidermal levels. Occlusive and emollient agents act by constructing hydrophobic layer subsequently preventing moisture loss, restoring the

flexibility and overall improving the texture of stratum corneum. Mild surfactants ensure effective cleansing without exacerbating barrier disruption. Antioxidants and anti-inflammatory agents offer supplementary protection by mitigating oxidative stress and inflammatory pathways implicated in chronic skin barrier dysfunction.

FUTURE PERSPECTIVE

Advancement in formulation strategies especially emerging trend in nano delivery offer discreet advantage to overcome existing limitation of dermal delivery. Diverse nano carrier systems such as lipid based vesicular systems, polymeric carriers and nano emulsions are well established for their stability of sensitive active molecules, enhanced dermal permeation, controlled, targeted, and retainable delivery within specific skin layers. These delivery systems facilitate the co-delivery of multiple active agents necessary to address complex etiology of dry skin.

Future investigations should emphasize the integration of skin dysfunction mechanisms with evidence-based combinations of active ingredients to target multifactorial abnormalities, followed by the development of advanced formulations capable of adapting to variations in skin pH, hydration levels, and inflammatory states, ultimately facilitating the development of next-generation therapeutic systems.

CONCLUSION

Addressing the dry skin condition requires both holistic and biochemical approach to restore structural and biochemical dysfunction. Insights into skin biology such as microbiome dynamics, lipidomics, and molecular signalling pathways integrating with pharmaceuticals, and material science is crucial in developing advanced targeted and personalized therapeutic interventions. Synergistic integration of active compounds and their targeted delivery ensure effective and prolonged management of dry skin condition may significantly enhance treatment precision, efficacy, and patient adherence.

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