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Review Article

Impact of formulation excipients on skin barrier functions: A review

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ABSTRACT

The skin serves as the primary barrier protecting the body from external insults, and its integrity is crucial for overall health. Formulation excipients, including emulsifiers, thickeners, and preservatives, commonly used in skincare products, can significantly influence skin barrier function and permeability. This review evaluates the impact of these Excipients on skin barrier function using biophysical measurements such as Trans-epidermal Water Loss (TEWL), skin hydration, and trans-epidermal water content. Furthermore, it discusses the potential implications of excipient-induced alterations in skin barrier function for skin health and tolerability.

1. Introduction

The skin is the largest organ of human body, works as a barrier between our internal and the external environment. Its primary function is to protect the body from various environmental stressors such as pathogens, chemicals, UV radiation, and mechanical injury. The integrity of this barrier is crucial for maintaining overall health and well-being. [1–10]

1.1. Skin as a barrier

The skin is a complex structure composed of several layers with its unique characteristics and functions. These layers work together to provide protection, regulate hydration, and maintain overall skin health.

Layers of the skin barrier:

1. ***Stratum Corneum*** **:** Stratum Corneum is the outermost layer of the epidermis and serves as the primary barrier against external threats. It consists of dead skin cells called corneocytes embedded in a lipid matrix. The corneocytes are connected by protein structures known as corneodesmosomes. Lipids, primarily ceramides, cholesterol, and fatty acids, form the lipid matrix, providing waterproofing and preventing water loss from the skin.
2. ***Stratum Granulosum:*** Beneath the stratum corneum lies the stratum granulosum, where keratinocytes undergo various changes in morphology and composition. Keratinocytes in this layer produce keratohyalin granules, which contain proteins that contribute to the formation of the skin's barrier. Additionally, the stratum granulosum plays a role in lipid synthesis and secretion, contributing to the lipid barrier of the stratum corneum.
3. ***Stratum Spinosum:*** The stratum spinosum is characterized by polygonal-shaped keratinocytes connected by desmosomes, which provide structural support and integrity to the epidermis. This layer is involved in the synthesis of structural proteins, such as keratin, which strengthen the skin barrier and contribute to its resilience.

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4. **Stratum Basale (Basal Layer):** The stratum basale is the deepest layer of the epidermis and is primarily composed of proliferating keratinocytes. These cells undergo mitosis and continuously migrate upwards to replenish the upper layers of the epidermis. The stratum basale also contains melanocytes, which produce melanin, the pigment responsible for skin color and protection against UV radiation.
5. **Epidermal-Dermal Junction:** The epidermal-dermal junction is the interface between the epidermis and the underlying dermis. It consists of specialized structures, including hemidesmosomes and anchoring fibrils, which anchor the epidermis to the dermis and provide structural support. This junction plays a crucial role in maintaining the integrity and stability of the skin barrier.

These layers work together to form a sophisticated barrier system that protects the body from external insults while regulating hydration and preventing water loss. Disruption of any of these layers can compromise the skin barrier function, leading to various dermatological conditions and skin disorders. Understanding the structure and function of the skin barrier is essential for developing effective skincare strategies and treatments aimed at maintaining skin health and integrity.[11–15]

2. Functions of the skin barrier

In addition to its physical barrier function, the skin also regulates the passage of water and other molecules through a process known as trans-epidermal water loss (TEWL) and trans-epidermal permeability. This regulation is critical for maintaining skin hydration and preventing dehydration.

1. **Trans-epidermal water loss (TEWL):** TEWL refers to the process by which water evaporates from the skin's surface into the surrounding environment. It is a measure of the rate at which water vapor diffuses through the stratum corneum, the outermost layer of the epidermis. TEWL is influenced by various factors, including environmental conditions (such as temperature and humidity), skin hydration levels, and the integrity of the skin barrier. High TEWL rates indicate increased water loss from the skin, which can lead to dehydration and dryness. Conversely, low TEWL rates suggest an intact and well-functioning skin barrier that effectively retains moisture.
2. **Trans-epidermal permeability:** Trans-epidermal permeability refers to the ability of substances to penetrate the skin and pass through the epidermis into the underlying layers or bloodstream. The skin barrier acts as a selective barrier, allowing certain molecules to pass through while blocking others. Trans-epidermal permeability is influenced by factors such as the molecular size, lipophilicity, and charge of the substances, as well as the integrity of the skin barrier. Disruption of the skin barrier, either by physical damage or through the use of chemical agents, can increase trans-epidermal permeability, allowing potentially harmful substances to penetrate the skin and cause irritation, sensitization, or systemic effects.

Both TEWL and trans-epidermal permeability are important parameters used in dermatology and skincare research to assess the function and integrity of the skin barrier. Monitoring these parameters helps researchers and clinicians understand how various factors, such as environmental conditions, skincare products, and underlying skin conditions, affect skin barrier function and overall skin health. Additionally, interventions aimed at reducing TEWL and maintaining optimal trans-epidermal permeability can help improve skin hydration, protect against external insults, and prevent skin disorders.[16–20]

3. Regulation of Skin barrier

The skin barrier is regulated by various factors, including genetics, environmental factors, and skincare practices. Disruption of this barrier can lead to a range of dermatological conditions, including dryness, inflammation, infections, and allergic reactions. The skin regulated by a multitude of these factors. Each of these factors plays a significant role in maintaining the integrity and functionality of the skin barrier

1. **Genetics:** Genetic factors heavily influence the structure and function of the skin barrier. Variations in genes encoding proteins involved in epidermal differentiation, lipid synthesis, and barrier formation can impact the resilience and effectiveness of the skin barrier. Individuals with certain genetic predispositions may have a compromised skin barrier, making them more susceptible to dermatological conditions such as eczema, psoriasis, or ichthyosis.
2. **Environmental Factors:** Environmental factors encompass a wide range of influences, including UV radiation, pollution, temperature, humidity, and air quality. Prolonged exposure to UV radiation, for example, can damage the skin barrier by inducing oxidative stress, inflammation, and DNA damage. Similarly, exposure to pollutants and harsh chemicals can disrupt the lipid matrix of the stratum corneum, compromising its ability to retain moisture and protect against external insults.
3. **Skincare Practices:** Skincare practices, including cleansing, moisturizing, and the use of topical treatments, can either support or undermine the integrity of the skin barrier. Overuse of harsh cleansers or exfoliants can strip away natural oils and disrupt the pH balance of the skin, leading to dryness,

irritation, and barrier dysfunction. Conversely, using gentle cleansers, hydrating moisturizers, and barrier-repairing ingredients such as ceramides and fatty acids can help fortify the skin barrier and maintain its health and resilience.

Additionally, other lifestyle factors such as diet, stress, hormonal fluctuations, and underlying health conditions can also influence skin barrier function. For example, a diet rich in antioxidants and essential fatty acids can support skin health by reducing inflammation and promoting lipid synthesis. Conversely, chronic stress or hormonal imbalances can exacerbate skin conditions and impair barrier function.

Overall, maintaining a healthy skin barrier requires a holistic approach that addresses genetic predispositions, minimizes exposure to environmental stressors, and adopts skincare practices that support barrier integrity. By understanding and addressing the various factors that regulate skin barrier function, individuals can promote healthy, resilient skin and reduce the risk of dermatological issues. To understand the structure and function of the skin barrier is essential for developing skincare products and treatments that support its integrity and promote skin health.

4. Impact of Excipients on Skin Barrier Function

1. **Emulsifiers:** Emulsifiers are commonly used in skincare formulations to stabilize oil-in-water or water-in-oil emulsions. While emulsifiers can improve the texture and spreadability of products, they may also disrupt the lipid bilayers of the stratum corneum, leading to increased TEWL and decreased skin hydration. Additionally, some emulsifiers have been associated with skin irritation and allergic reactions, further compromising skin barrier function.
2. **Thickeners:** Thickeners are additives used to increase the viscosity and consistency of skincare products. While thickeners can enhance product aesthetics and user experience, certain thickening agents may form occlusive layers on the skin surface, impairing natural desquamation and hindering the skin's ability to regulate moisture. This can result in decreased skin hydration and compromised barrier function over time.
3. **Preservatives:** Preservatives are essential for preventing microbial contamination and extending the shelf life of skincare products. However, certain preservatives, such as parabens and formaldehyde releasers, have been linked to skin sensitization and allergic reactions. Prolonged exposure to these preservatives can disrupt the skin barrier and compromise its ability to maintain homeostasis.
4. **F ragrances:** Fragrances are commonly added to skincare products to enhance their scent. However, fragrances, both synthetic and natural, can be irritating to the skin and disrupt the skin barrier. Fragrance ingredients such as limonene and linalool have been associated with allergic contact dermatitis and can compromise skin barrier function, leading to increased sensitivity and inflammation.
5. **Humectants:** Humectants are ingredients that attract water and help maintain skin hydration. Examples include glycerin, hyaluronic acid, and propylene glycol. While humectants can improve skin hydration, excessive use or high concentrations of humectants may draw water from deeper layers of the skin, leading to increased TEWL and impaired barrier function, especially in low humidity environments.

Biophysical Measurements and Implications for Skin Health: Biophysical measurements, including TEWL, skin hydration, and trans epidermal water content, provide valuable insights into the effects of formulation excipients on skin barrier function. Increased TEWL and decreased skin hydration indicate impaired barrier integrity, which may predispose the skin to various dermatological issues. Furthermore, alterations in trans epidermal water content can affect the skin's bio mechanical properties and overall health.

These are the examples how various excipients commonly used in skincare formulations can impact skin barrier function. Understanding the effects of these excipients on the skin barrier is essential for formulators to develop products that are both effective and safe for long-term use. Balancing the benefits of excipients with their potential adverse effects on skin barrier function is critical for maintaining skin health and integrity.

5. Conclusion

Formulation excipients play a significant role in modulating skin barrier function and permeability. While these additives can enhance the sensory attributes and stability of skincare products, their impact on skin health and tolerability should be carefully evaluated. Biophysical measurements offer a reliable means of assessing the effects of excipients on skin barrier function, aiding in the development of safer and more efficacious skincare formulations. Further research is warranted to elucidate the mechanisms underlying excipient-induced alterations in skin barrier function and their implications for long-term skin health.

6. Source of Funding

None.

7. Conflict of Interest

None.

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