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Supporting Skin Structure and Its Barrier Functions with Evidence-Based Skin Care Ingredients

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Abstract

The epidermis, and in particular its outermost layer, the stratum corneum, contributes much of the barrier function of the skin and is a readily visible representation of skin health. Maintaining the health of the skin barrier has arguably become more important than ever in the modern world, in which a large majority of people are exposed to environmental insults. These external factors can damage the integrity of the skin barrier and prematurely age the skin. Therefore, it has become increasingly important to maintain and protect the stratum corneum. Here, we briefly review the complex, multilayered structure of the skin and relate it to clinically translatable function, with an emphasis on the stratum corneum. In the context of epidermal structure and function, the formulation and clinical data for Phelityl® Reviving Cream will be reviewed. Phelityl Reviving Cream was shown to be associated with improvements in both immediate- and long-term parameters, including a significant positive effect on the skin barrier and immediate and long-lasting hydration.

Keywords

Skin Structure, Skin Barrier, Stratum Corneum, Phelityl Reviving Cream, Phelityl Complex

1. Skin Homeostasis: A Brief Review of Skin Barrier Structure and Function

The skin barrier is a multifunctional structure with critical roles in the defense against environmental assault, maintaining homeostasis, as well as being the structure that reflects our outward appearance to the world. Preserving the epidermal barrier—the stratum corneum—is a priority for proper skin function and appearance.

1.1. The Epidermis

The functionality of the epidermis extends far beyond simply forming an interface between the body and the environment, with roles in sensation, maintaining water content, defending against and responding to infection, photoprotection, and responding to and ameliorating oxidative stress, along with crucial regulatory, metabolic, and excretory functions [1]. Among all of the body's organs, the skin is the primary barrier and is most exposed to environmental insult from microorganisms, physical injury, temperature extremes, chemical pollution, and ultraviolet (UV) light. Its remarkable ability to self-repair is an essential element of healthy skin function for people of all ages, and progressive compromise of the skin barrier is common as individuals age, as well as in patients with dermatologic and certain systemic disorders [2].

The outermost epidermal layer—which is visible to the observer and functions as a protective barrier to the skin—is the stratum corneum (**Figure 1**) [3]. The stratum corneum, only 10- to 20-ug thick [4], is composed of up to 30 layers of metabolically inactive, keratin-filled corneocytes that are shed at a rate approaching 50,000 cells per minute [3]. The spaces between these cells are filled with a lipid-laden extracellular matrix. Far from being just a dead, dry layer, the healthy stratum corneum also contains about 20% to 25% water under average conditions, with water content changing dynamically in response to the humidity of the environment and the use of topical products [5].

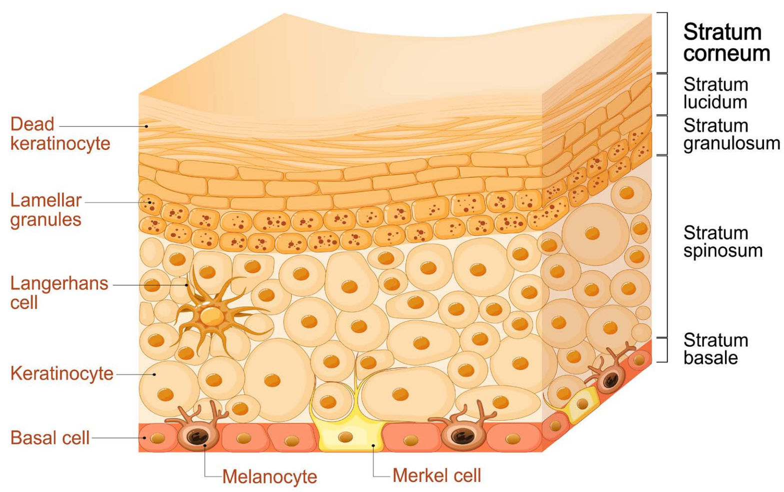

Figure 1. Epidermal structure.

1.2. Focus on the Stratum Corneum

The stratum corneum has a "brick-and-mortar" composition, with the corneocytes forming the bricks and the extracellular matrix forming the mortar (**Figure 2**) [6]. The corneocytes are connected by corneodesmosomes that contribute to

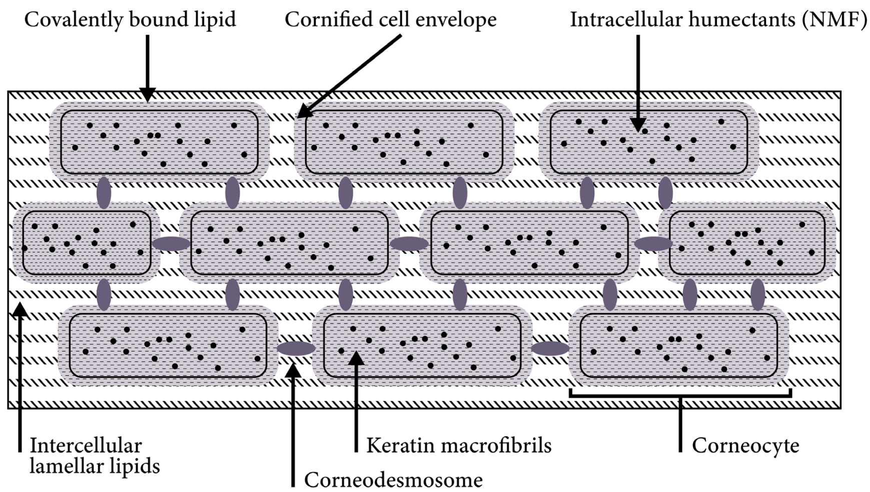

Figure 2. "Brick-and-mortar" structure of the stratum corneum [9]. NMF, natural moisturizing factor.

its resistance to mechanical stressors and selective permeability [6]. It is primarily composed of protein (75% - 80%) and is rich in a variety of lipids that provide structural support and act as a barrier [7]. Ceramides, cholesterol, and fatty acids are the main lipid components of the extracellular space and are present in an approximate ratio of 3:1:1 [7] [8]. Collectively, the relative composition of these lipids is necessary to maintain proper hydration of the skin and regulate transepidermal water loss (TEWL) [8].

Ceramides constitute about half of the stratum corneum lipids [7]. These molecules consist of an amino acid containing sphingoid base linked to a hydrophobic fatty acid chain [7]. Not only do ceramides help form the lamellar barrier of the skin, maintain skin moisture, and prevent ingress of microbes, but they also act intracellularly as second messengers for a broad range of processes [10]. Cholesterol constitutes about one-quarter of the stratum corneum lipids [7]. It maintains the fluidity and rigidity of cell membranes and is, along with ceramides, critical to the ability of the stratum corneum to function as a barrier [7]. Fatty acids, most but not all of which are synthesized de novo by keratinocytes, comprise an additional 10% to 15% of the stratum corneum lipid content [8] [11]. These compounds are known to modulate skin-surface pH, helping it maintain its natural acidity, and to contribute to the regulation of permeability, the antimicrobial properties of the skin, and the inflammatory response [11]. In addition to the fatty acids synthesized by keratinocytes, the essential fatty acids (EFAs) linoleic acid and α-linolenic acid are critical elements of both the epidermis and dermis. These essential compounds are unique among the fatty acids in that they must be supplied by the diet or exogenously by topical application and are the parent compounds for more than 30 derivatives that are critical for healthy skin, as illustrated by early studies showing that deficiencies manifest as dermatitis and increased TEWL [12] [13].

Along with ceramides, fatty acids, and cholesterol, the stratum corneum contains natural moisturizing factor, which is a combination of small, water-soluble compounds from filaggrin, sweat, and the process of triglyceride turnover in the sebaceous glands [14]. This combination of compounds is approximately 10% of the dry weight of corneocytes in the stratum corneum and also includes various amino acids and amino acid derivatives (e.g., pyrrolidone carboxylic acid and urocanic acid), lactic acid, sugars, urea, glycerol, and different ions [14].

Lipids supplied by the sebum—produced by sebaceous glands—are also present on the skin surface. Sebum consists of squalene, triacylglycerols, and wax esters and is present at the highest levels on the forehead, upper chest, and upper back [7]. Squalene, an intermediate in cholesterol biosynthesis, is a particularly potent natural emollient that is absorbed efficiently by the skin and helps preserve suppleness and flexibility [15]. Squalene also has a protective role, quickly neutralizing free radicals and protecting the skin against oxidative damage [15].

1.3. Normal Functions of the Stratum Corneum

The stratum corneum has 3 main functions: providing a selectively permeable barrier, protecting against UV light, serving as the first line of defense against pathogens and initiating the immune response to these microorganisms, quenching free radicals, and serving as a home for a diverse array of commensal skin microbiota [8] [16].

Barrier and Homeostatic Functions

The most well understood role of the skin is to function a selectively permeable physical barrier from the external environment. The multiple layers of corneocytes that comprise the bricks of the stratum corneum, together with the glycolipids that serve as the mortar, maintain proper cutaneous water balance by preventing excess TEWL [16]. Healthy skin is critical for maintaining body temperature to avoid uncontrolled water and solute loss [3].

Photoprotection

The skin barrier is the primary site of exposure to UV radiation, and solar UV radiation (primarily UVA and UVB) is the primary driver of skin photoaging [17]. Damage to the skin by UV radiation can be mediated by direct absorption of radiation by nuclear DNA, causing specific mutations in the skin genome. Indirect damage also may occur if UV is absorbed into other skin constituents, leading to the production of reactive oxygen species followed by the formation of DNA photoproducts, in addition to characteristic alterations in cellular proteins and membranes [17]. The skin contains an exquisite set of enzymatic pathways to continuously repair the damage caused by UV radiation and other environmental insults. Without proper care, the skin accumulates UV damage over time, leading to manifestations ranging from benign damage (wrinkling) to cancers [17].

Antimicrobial Functions

The stratum corneum is the first line of defense against many microbes and contains multiple mechanisms to prevent colonization by pathogens. It responds to those that manage to survive the harsh environment of the skin and primes the downstream immune response. The first line of defense is the acid mantle—a pH that is maintained in healthy skin of between 5.4 and 5.9—a range that is inhospitable for many potential pathogens but is tolerated by commensal bacteria [18]. The skin also produces a number of antimicrobial peptides that can be present constitutively or produced in response to inflammatory stimuli [18]. The defensins and cathelicidins (produced by keratinocytes, sweat glands, and sebaceous glands, among other sites) and dermcidin (expressed by sebocytes) have broad bactericidal activity against microbes and also may help initiate the immune response [18]. Certain skin lipids also have intrinsic antimicrobial activity against *Staphylococcus aureus*, *Streptococcus pyogenes*, and *Propionibacterium acnes*, among other bacterial species [3] [18] [19].

Antioxidant

UV radiation (discussed earlier), air pollution, and other environmental pollutants are well understood to cause oxidative stress. After entering the skin as nanoparticles, air pollutants can produce reactive oxygen species that negatively impact the enzymatic and nonenzymatic activities of the skin and stimulate the release of proinflammatory mediators, among other negative effects [2]. The skin contains an endogenous network of enzymatic and nonenzymatic systems to counter oxidative stress by quenching free radicals generated by environmental insults [8].

Host to the Skin Microbiota

The skin also hosts a diverse array of bacteria, fungi, and viruses that collectively compose the skin microbiota, the composition of which varies substantially depending on the local physiology of the skin [20]. Colonization by pathogenic microbes is prevented by commensals on the surface of the skin; furthermore, there is evidence that crosstalk between the immune system and microbiota assists in the maintenance of the normal microbial composition of the skin and to eliminate pathogens [20]. The normal microbiota not only defends against potentially harmful microorganisms but can also produce substances that are directly beneficial for the skin. For example, data suggest that commensal *Staphylococcus epidermidis* produces protective ceramides that contribute to skin barrier homeostasis, and thus help to prevent skin dehydration and aging [21].

1.4. Importance of Maintaining the Skin Barrier

As discussed, the skin barrier has a multifunctional role which includes protection against environmental insults and maintaining homeostasis. It is the outwardly visible component of skin. Many of the functions of the epidermal skin barrier are the responsibility of the stratum corneum; thus, maintaining the stratum corneum is a priority for overall skin health.

In addition to exogenous factors, aging leads to changes in the biomechanical properties of the stratum corneum, such as stiffening of keratin fibers, increased cellular cohesion, and reduced water movement through the stratum corneum, which can compromise its integrity [22]. In addition, quantities of all 3 major classes of skin lipids—ceramides, cholesterol, and fatty acids—also decline notably with age and compromise of the protective function of the skin [23]. Furthermore, the pH of the stratum corneum increases with age; as this occurs, serine protease activity increases and corneodesmosome density is reduced [24].

Several modifiable risk factors for poor skin barrier function can be readily addressed with appropriate routine skin care, including gentle cleansing, using topical products designed to moisturize and support skin barrier function, and avoiding unnecessary environmental exposure, the use of irritating topical products, and extended exposure to low-humidity environments [25]. Conversely, without proper attention, the stratum corneum may not provide adequate protection, resulting in visible and invisible manifestations such as dry, flaky skin, itching, and irritation.

2. Phelityl Reviving Cream

The science underlying the structure and function of the skin barrier was carefully considered in the development of Erno Laszlo's Phelityl Reviving Cream.

Central to the product formulation is the Phelityl Complex, a blend of botanical substances with evidence-based benefits on skin barrier health, which was combined with other key ingredients to support the skin barrier and enhance hydration.

Phelityl Complex

The Phelityl Complex is composed of a blend of botanical substances, including acacia gum, biopolymers, plant-derived polyglycerides, and rosehip oil, along with squalene and ceramides.

Phelityl Reviving Cream Key Components

- Phelityl Complex
    - Biobotanical blend
        - Acacia gum biopolymer
        - Plant-derived polyglycerides
        - Rosehip oil
    - Squalane
    - Ceramides
- Red algae
- African tree extract and oleanolic acid blend
- Glycerin

Acacia gum (also known as gum Arabic) is an exudate gum produced by the *Acacia senegal* tree and a primary ingredient in Phelityl Complex. Acacia gum is among the oldest substances used by humans, with the first recorded use over 5000 years ago. In clinical studies, acacia gum was shown to improve skin barrier and hydration [26].

The plant-derived polyglycerides and rosehip oil in the Phelityl Complex each contribute EFAs to the formula. The mixture of polyglycerides is of 100% vegetable origin and includes oleic, linoleic, and linolenic fatty acids, the latter 2 of which are the parent fatty acids of the omega-6 and omega-3 series of EFAs [27]. Rosehip oil, an extract prepared from *Rosa damasca*, contains high amounts of essential polyunsaturated fatty acids derived from linoleic, linolenic, and arachidonic acids [28].

Squalene is a triterpene intermediate in the cholesterol biosynthesis pathway [15]. In humans, squalene is present in the highest concentrations in the skin, where it is produced in abundance by the sebaceous glands and constitutes approximately 13% of sebum [15]. Squalane, a hydrogenated derivative of squalene, is a powerful emollient and is absorbed into the skin, where it plays an important role in maintaining the suppleness and flexibility of the skin [15]. Beyond its emollient properties, squalane contributes to the ability of Phelityl Reviving Cream to limit TEWL [15]. Phelityl Reviving Cream incorporates a squalane sourced from renewable sugarcane.

Finally, the Phelityl Complex contains a ceramide blend. Ceramides are the predominant lipid in the stratum corneum and help maintain moisture levels in the skin [7] [29].

Additional Key Constituents of Phelityl Reviving Cream

Phelityl Reviving Cream contains an extract from red algae (*Porphyridium cruentum*). The marine exopolysaccharide derived from this organism contributes to the long-lasting moisturizing properties of Phelityl Reviving Cream, and its high molecular mass contributes to its film-forming properties, which together help to preserve and maintain skin hydration for extended periods [26] [30] [31].

In addition to red algae, Phelityl Reviving Cream contains a blend composed of extracts from the African tree *Enantia chlorantha*, in combination with oleanolic acid. In particular, extracts from this plant have been reported to regulate sebocyte differentiation and proliferation and to mildly inhibit 5α-reductase activity in the skin, leading to a reduction in sebum secretion [26].

Finally, glycerin, is a natural humectant that helps hydrate the stratum corneum and may protect the skin from irritants [32].

The effect of Phelityl Reviving Cream on key skin parameters was evaluated in a study in which female subjects (N = 31) aged 20 to 60 years, who had predominantly combination face skin type, applied the product to their face twice daily for 56 days. A broad range of skin parameters were measured by standard instrumental methods, including skin barrier (TEWL), hydration, sebum on skin surface, and skin pH. A forearm portion of the study assessed hydration when comparing treated and untreated areas immediately after application and after 24 hours following a single application. A subject questionnaire collected self-reported feedback about skin hydration, skin finish, and overall satisfaction with the product results. The use of Phelityl Reviving Cream was associated with statistically significant improvements in a broad range of parameters, including skin barrier (TEWL), hydration, and sebum on the skin surface, while helping maintain a physiologic acidic skin pH [26]. Specifically, there were statistically significant results including a decrease in TEWL ($P < 0.0001$), an increase in hydration ($P < 0.0001$), and a decrease in skin surface sebum ($P < 0.0001$) compared with baseline. The skin's acidic pH was maintained with no change throughout the study. On the forearm portion of the study for assessing hydration, when comparing treated and untreated areas, there were statistically significant increases in hydration immediately after application ($P < 0.0001$) and after 24 hours following a single application ($P < 0.0001$). In the subject questionnaire, 97% of the subjects reported that their skin felt hydrated after use, 90% reported that the product left a soft matte finish, and all the subjects were satisfied with the results.

3. Conclusions

The stratum corneum performs a multitude of essential functions of the skin. Its health is at considerable risk in today's environment, with people exposed more than ever before to air pollution and other factors that can damage its structural and functional integrity [2] [33]. Carefully formulated topical products that can optimize skin barrier health and have long-lasting moisturizing properties are an important way to support the stratum corneum and overall skin health.

Phelityl Reviving Cream is formulated with ingredients that have synergistic benefits that, together, help strengthen the skin barrier and maintain skin hydration. The effects of Phelityl Reviving Cream were confirmed in a study in which Phelityl Reviving Cream was shown to be associated with improvements in both immediate- and long-term parameters, including a significant positive effect on the skin barrier and immediate and long-lasting hydration. Phelityl Reviving Cream also had a statistically significant effect on skin-surface sebum, consistent with subject reports that the product left a soft-matte finish to their skin. Together, these results indicate that Phelityl Reviving Cream provides important skin benefits, including supporting the skin barrier and enhancing hydration, to help maintain healthy looking skin.

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Conflicts of Interest

Marsha Tharakan, MD, DDS, is a scientific and clinical consultant for Erno Laszlo.

Lori Lonczak, RPh, is a medical communications consultant for Erno Laszlo.

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