

Modern Moisturizer Myths, Misconceptions, and Truths

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Xerosis is a highly prevalent condition that can be caused by environmental factors, age, or various diseases. Although the causes, symptoms, and severity of dry skin vary widely, moisturizers form the mainstay of treatment in simple cases and can be used as adjunctive therapy in more serious clinical cases. The market now contains a plethora of moisturizing formulations from which consumers can choose, but dermatologists need to distinguish among marketing claims, anecdotal evidence, and proven clinical effects when recommending moisturizers to their patients. Many lesser-quality moisturizers were never designed to mitigate dry skin or more serious skin conditions in a therapeutically relevant manner and are unlikely to provide clinically adequate moisturizing therapy. This article aims to clarify some common prevailing myths and misconceptions about moisturizers in the dermatology community. Recent advances in research have revealed that natural moisturizing factor (NMF), ceramides, and aquaporins (AQPs) are key factors in skin hydration. The impact of these advances on the ingredients that are being used in moisturizers is discussed, along with the importance of dermatologists choosing clinically proven products released by laboratories with demonstrated track records in research.

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Dry skin, or xerosis, is a common problem that most people experience to varying degrees at some stage in life. In some instances, the underlying cause may be a simple case of altered environmental factors (eg, seasons, climate, excessive bathing, use of harsh skin cleansers), while in others, endogenous factors such as deficiencies in the skin's natural moisturizing factor (NMF), barrier lipid content, or moisture network may be involved.¹ Because age is an important factor in the manifestation of xerosis,² it is likely that its incidence will increase in the aging populations of developed countries.

The use of moisturizers is the mainstay of xerosis therapy. Because the causes, symptoms, and severity of dry skin conditions vary greatly, the pharmaceutical and cosmetic industries have made available an ever-increasing number of prescription and over-the-counter moisturizing formulations. These products contain a wide range of functional ingredients, including emollients, humectants (eg, NMF, glycerin, sorbitol), ceramides and other barrier lipids, compounds that can stimulate the expression of different proteins, and lesser-known exotic constituents derived from marine and botanical sources. The range of ingredients has become more diverse as consumers access less conventional, small scale, local, and online sources.

Dermatologists should appreciate that the word *moisturizer* is a generic term used to encompass a multitude of formulations that vary widely in their capacity to provide therapeutically desirable effects such as barrier repair, reduced transepidermal water loss, or aesthetic improvement of irritated skin.

This article will review common classes of moisturizers that are available in the retail market as well as their appropriateness in treating both minor and major dermatologic problems; some common prevailing myths and misconceptions about moisturizers that do not necessarily translate into better patient outcomes also will be clarified. Finally, some of the new and important ingredients that are being used

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in moisturizers will be discussed as well as their relevance in selecting moisturizers and advising patients with xerosis, atopic dermatitis (AD), or a related dry skin condition.

Classes of Moisturizers

Moisturizers in the retail marketplace can, as a general rule, be classified into 4 main groups: emollient dominant, humectant based, occlusive, and therapeutic (Table 1). Thus not all moisturizers are the same and not all are intended to be therapeutic.

Emollient-dominant and light, humectant-based moisturizers may, in reality, merely provide fragrance or temporarily moisturize the skin without necessarily making it healthier. These products were never designed to mitigate dry skin or more serious skin conditions in a therapeutically relevant manner and are unlikely to provide clinically adequate moisturizing therapy for xerotic skin. Moreover, care should be taken when using these products on compromised or diseased skin, as fragrances, preservatives, and extracts can exacerbate AD in patients with symptoms of contact and inhaled allergies.³

Common Myths About Moisturizers

It is evident that a number of flawed and outdated concepts have been promulgated in the dermatology community. Some of the more common myths are addressed in Table 2. One common misconception is that a topical medicine serves as both an active vehicle and a moisturizer, which rarely is the case. It is critical that when dermatologists prescribe a topical medication, they also advise patients on the importance of adjunctive moisturizers and provide them with specific recommendations to optimize therapeutic outcomes.

Key Factors in Skin Hydration

Recent advances in knowledge about skin hydration have led to the development of new formulations with ingredients that specifically address the deficiencies in the physiologic mechanisms underlying xerotic conditions.

Natural Moisturizing Factor—The effects on skin hydration of NMF, a collection of humectant substances originating from the catabolism of filaggrin, were first described in 1959 by Jacobi.^{13,14} The role of NMF is to maintain adequate stratum corneum (SC) hydration, which in turn serves 3 major functions: (1) maintain plasticity of the skin, protecting it from damage; (2) allow hydrolytic enzymes to function in the process of desquamation; and (3) contribute to optimum SC barrier function.¹⁴

Natural moisturizing factor is principally composed of free amino acids and various derivatives

of these amino acids such as pyrrolidone carboxylic acid (PCA), urocanic acid (a natural absorber of UV light), inorganic salts and sugars, lactic acid, and urea.^{1,15} Natural moisturizing factor components are highly efficient humectants that attract and bind water from the atmosphere, drawing it into the corneocytes. Reductions in NMF levels have been correlated with various SC abnormalities that clinically appear as areas of dry skin with scaling, flaking, and sometimes fissuring and cracking. These conditions include AD, psoriasis, ichthyosis vulgaris, and xerosis. In AD and xerosis, NMF levels are reduced, while in psoriatic skin and ichthyosis, NMF is essentially absent.¹⁴

Replacing or replenishing the supply of NMF in the skin through the external application of NMF-containing moisturizers has been reported to successfully treat xerotic skin.¹⁶ Pyrrolidone carboxylic acid, the most prevalent single component of NMF, can be reduced in the outermost skin layers by washing with soap and/or aging. Topical application of PCA has been widely reported to alleviate the symptoms of dry skin. Notably, several NMF components have been used for decades; for instance, urea and lactate have been used in moisturizing creams since the 1940s.¹⁵ Topical application of urea, or its precursor arginine, has been shown to correct urea deficits in AD and elderly patients.^{17,18} Recently, urea also has been shown to stimulate the expression of several enzymes involved in ceramide synthesis and barrier formation as well as the aquaporin-3 (AQP3) water channel in human keratinocytes.⁹ Lactate has been shown to improve and prevent the reappearance of symptoms of dry skin compared with lactate-free moisturizers.¹⁵ L-lactic acid and D,L-lactic acid appear to work by stimulating the synthesis of ceramides in the SC.¹⁹

Ceramides and Barrier Lipids—The 3 main lipid groups in the SC are ceramides, free fatty acids, and cholesterol. Lipid synthesis occurs in the stratum granulosum where lamellar bodies are formed and packed and then exocytosed at the stratum granulosum–SC interface. At least 9 different classes of ceramides (1 to 9) have been described in the human SC, and of the total lipid mass present in the human SC, approximately 50% consists of ceramides, with 25% consisting of cholesterol and 15% of free fatty acids.^{20,21}

Ceramides play a fundamental role in skin barrier function, impeding water loss. Levels of ceramides 1 and 3 have been shown to be markedly reduced in AD patients compared with healthy controls, with increased transepidermal water loss.²⁰

Increased ceramide synthesis accompanying improved barrier function has been seen in numerous studies employing agents ranging from mixtures of

Table 1.

Classes of Moisturizers

Type	Characteristics	Observations	Ingredients
Emollient dominant	Typically used for “normal” skin; make the skin feel soft and smooth; designed to maintain skin condition; not designed to repair damaged skin or have long-term effects on the skin	Although usually labeled as lotions or body moisturizers, the goal of many of these products is to provide fragrance and soften the skin rather than to provide skin-moisturizing effects	Oils, lipids, and their derivatives (eg, stearic, linoleic, linolenic, oleic, and lauric acids; cetearyl alcohol; mineral oil; lanolin) ^{3,4}
Humectant based, light duty	Suitable for “normal” skin, maintenance of skin condition, and daily use; generally oil-in-water emulsions	Provide hydrating effects to the skin via humectants that attract and bind water from the deep epidermis and environment to impart hydrating benefits ⁵ ; absorb more quickly than occlusive formulations and therefore are more aesthetically pleasing, promoting patient compliance	Glycerin, sorbitol, urea, sodium lactate, lactic acid, carnitine, sodium PCA, arginine hydrochloride, serine, alanine, histidine, citrulline, lysine, sodium chloride, glycogen, mannitol, sucrose, glutamic acid, threonine ⁵
Occlusive protective	Typically used on dry and/or damaged skin; formulation types include ointments and often are water-in-oil lotion or cream emulsions; provide an occlusive barrier that reduces transepidermal water loss and protects irritated inflamed skin from external irritants to promote moisture retention and allow barrier repair ⁶	Because of their occlusive nature, they are sometimes less aesthetically pleasing than oil-in-water emulsions, which can impact compliance; effective in improving the ashen powdery appearance of dry skin	Skin-protectant actives (eg, petrolatum, dimethicone, lanolin, mineral oil); occlusive hydrophobic ingredients (eg, olive oil, soybean oil, beeswax, jojoba oil) ¹
Therapeutic	Formulated to treat xerosis and diseased skin conditions with a xerotic component; generally contain a balance of occlusives for barrier support, emollients to soften and smooth skin, and humectants to provide water to the stratum corneum ⁶	Better-constructed moisturizers due to their balanced composition of multifunctional ingredients that protect, hydrate, and support endogenous barrier repair processes	Emollients, occlusives, humectants/NMF, ceramides

Abbreviations: PCA, pyrrolidone carboxylic acid; NMF, natural moisturizing factor.

ceramides, cholesterol, and fatty acids, to lipid precursors, α -hydroxy radicals, and humectants, including glycerol and urea.^{6,8,9}

Aquaporins—Aquaporins (AQPs) are a ubiquitous family of channels responsible for transporting water. In mammals, 13 AQPs have been identified, with

Table 2.

Common Moisturizer Myths

Myth	Fact
All moisturizers are essentially the same.	Many types of moisturizers with different ingredients, purposes, and outcomes are available. Some have virtually no therapeutically relevant moisturizing effects, while others provide much better outcomes.
Creams are more efficacious moisturizers than lotions.	Creams are simply more viscous emulsion systems than lotions, which does not mean that the active ingredient(s) are more concentrated or that the product film better protects against transepidermal water loss. The inclusion of highly effective humectants and agents that promote barrier repair largely determines product efficacy regardless of viscosity. Further, advancements in formulation technology allow superior efficacy to be achieved in lighter-weight lotion formulations, which can be more pleasing to use and promote patient compliance.
Topical medications provide both drug and moisturization benefits.	Medicinal creams and lotions are designed as delivery vehicles, often containing penetration enhancers that open up the stratum corneum to allow penetration of the medicine to achieve the desired clinical effect; however, penetration enhancers can damage the skin barrier, causing more water loss. ⁷ Moisturization should be an adjunct to therapy to help support and improve the barrier condition when using topical drugs.
Only ceramides can repair a disrupted skin barrier.	Ceramides are an essential part of barrier function; however, dry skin can have a variety of causes, and adding ceramides to a topical formulation is not the only way to repair a disrupted barrier. Ingredients such as lactic acid and urea have been shown to stimulate endogenous ceramide production. ^{8,9} Acidic product formulations that reestablish and preserve the acid mantle or restorative protectant topicals formulated with cholesterol, fatty acids, and other hydrophobic ingredients can help limit exogenous stress, tipping the balance to allow the skin's repair mechanisms to restore barrier health.
The ratio of ceramides within a moisturizer is important.	It is scientifically unclear if an ideal ratio of ceramide classes exists, either within healthy skin or in efficacious moisturizers.
Medical device barrier creams have superior efficacy to nonprescription therapeutic moisturizers.	Several studies have shown comparable efficacy of over-the-counter-quality therapeutic moisturizers versus medical device barrier creams, with an inferior cost-efficacy relationship. ^{10,11}
"Natural" products are better.	In the United States, the term <i>natural</i> is not federally regulated; there are no guidelines or rules regarding when or where the term can be used. Natural extracts are not a single purified component but often are complex concentrates with trace amounts of unintended components. Therefore, the composition is frequently dependent on the supplier and the manufacturing process. ¹²
Older, more common ingredients are not efficacious.	Older ingredients have demonstrated efficacy and safety. Although new and unique ingredients may have value, the dermatologist should always demand clinical evidence of safety and efficacy before abandoning tried-and-true formulations.

differences related to transport capabilities, location, and function.²²

The most abundant AQP present in the skin is AQP3, which is located in the plasma membrane of epidermal keratinocytes. Aquaporin-3 is an aquaglyceroporin, meaning that it transports both water and glycerol. Aquaporin-3 transports glycerol into the SC where it acts as an endogenous humectant. Glycerol pulls water with it, creating a reservoir effect, thereby enhancing the water-holding capacity of the skin. Aquaporin-3 knockout mice present with reduced glycerol content in the SC and inflamed xerotic skin.²³

Aquaporin-3 distribution in the skin reflects the epidermal water allocation and water gradient throughout the epidermis. The expression of AQP3 channels in human skin is strongly affected by aging and long-term sun exposure, with substantially decreased levels of AQP3 in both, thereby accounting for the heightened incidence of xerosis in older individuals² and/or those with skin areas that have been chronically exposed to sunlight.²⁴ Aquaporin-3 levels also have been shown to be decreased in psoriatic lesions, with keratinocytes from these lesions demonstrating compromised glycerol transport activity.²⁵

Decreased AQP3 expression has been implicated as a contributing factor in a range of skin diseases.²⁶ Consequently, the search currently is underway for compounds that can stimulate AQP3 expression and thereby improve the hydration state of the skin by endogenous means. Various reports of stimulants of AQP3 expression have been published recently. The herbal medicine byakkokaninjinto, an extract from the bark of *Piptadenia colubrina* (a native leguminous tree from South America), and an extract of *Ajuga turkestanica* (a plant from Central Asia) have been reported to increase AQP3 messenger RNA and/or protein levels in the skin tissue.²⁷⁻²⁹ Even urea, utilized for decades by dermatologists to treat xerosis and a key ingredient in a plethora of products, has been demonstrated to stimulate AQP3 expression in keratinocytes.⁹

In clinical studies, the compound glyceryl glycoside, a chemical derivative of glycerol, has been shown to promote epidermal AQP3 messenger RNA and protein upregulation and improve skin barrier function in humans. Its inclusion in moisturizing lotions may offer an effective treatment option for dehydrated skin.^{16,30}

Choosing a Moisturizer for Treatment of Dry Skin Conditions

Healthy skin renews itself continually, regenerating and differentiating keratinocytes that ultimately form the compacted corneocytes of the SC and the

lamellar barrier lipids that are critical to the skin's protective functions. This renewal process usually can compensate to maintain the barrier's protective function despite environmental challenges. Dry skin occurs when the barrier formation and repair processes are overwhelmed by environmental exposure or pathology and the skin can no longer repair itself.

In dry skin conditions such as xerosis, AD, psoriasis, and others, therapeutic moisturizers that support and promote self-repair are recommended for daily use. In conditions characterized by recurrent flare-ups, moisturization is recommended to decrease the frequency of flares; as adjunctive treatment to medicinal therapy, moisturizers protect and give the skin barrier the best chance of healing.

If the underlying deficiency is known, a moisturizer can be selected to specifically address the cause. Approximately 20% to 25% of patients with atopic dermatitis have one of a spectrum of filaggrin gene defects,³¹ which would impact the production of the epidermal NMF. Thus recommending a moisturizer that includes NMF components such as sodium, potassium, and ammonium lactates (AmLactin Lotion and Cream, Upsher-Smith Laboratories, Inc); sodium lactate and urea (Eucerin Repair Lotions and Cream, Beiersdorf Inc); or arginine and sodium PCA (Cetaphil Restoraderm, Galderma Laboratories, LP) likely would be a beneficial approach for these patients.

Without knowing the specific underlying cause of dry skin, choosing a product that addresses multiple known contributory factors may help eliminate some trial and error. These moisturizers should provide a balance of protective components and ingredients that hydrate, support endogenous barrier repair mechanisms, and restore the skin to a balanced state. A well-constructed moisturizer should contain the key factors for hydration, which include NMF and ceramides (and/or ingredients that have been shown to stimulate ceramide and barrier lipid synthesis), and modulators or enhancers of AQP expression and activity. However, many products may not contain physiologically relevant concentrations of ceramides or NMF humectants. Therefore, it is recommended that therapeutic moisturizers should be selected based on proven clinical benefits demonstrated in controlled studies from reputable laboratories and companies. Recently, many moisturizers have been produced featuring the barrier restorative properties of ceramides. They can contain one or more ceramide moieties that are endogenous to the skin (CeraVe Cream and Lotions, Valeant Pharmaceuticals North America LLC; Eucerin Smoothing Repair and Professional Repair, Beiersdorf Inc); synthetic derivatives of naturally occurring ceramides (Curel Ultra Healing,

Kao USA Inc); or ceramide precursors such as hydroxypalmitoyl sphinganine, which are claimed to be converted to ceramides once applied to the skin (Cetaphil Restoraderm, Galderma Laboratories, LP).

A new line of well-constructed moisturizers contains NMF, ceramide, and AQP modulators in a light formulation (oil-in-water) and a rich formulation (water-in-oil)(Eucerin Smoothing Repair and Eucerin Professional Repair, respectively; Beiersdorf Inc).¹⁶ These multidimensional products contain numerous NMF components, including urea, lactate, arginine, and 8 other amino acids, as well as ceramide 3 and glyceryl glucoside. They are probably the first moisturizers that address the 3 key factors critical for skin hydration and operative in self-repair mechanisms of damaged skin.

Conclusion

There are many types of moisturizers available that contain a plethora of ingredients. Although some of these moisturizers offer little more than fragrance or temporary short-term moisturizing properties, dermatologists need to pay particular attention to the specific therapeutic moisturizers they choose for the treatment of xerosis, and adjunct therapy for other drug-treated skin conditions such as AD and psoriasis. Such moisturizers should contain NMF, ceramides, and AQP modulators to protect and hydrate the damaged skin barrier and encourage the endogenous self-repair mechanisms. Due to the complexity of formulations, multidimensional products represent a more complete approach and the latest advances in the treatment of dry skin conditions.

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