Smoothing Out Our Understanding of Moisturizers

New science and new approaches for dry skin.

BY MARGARET DENNIN, BS AND PETER A. LIO, MD

The skin provides the essential functions of serving as a permeability barrier, protecting against desiccation, and responding to environmental stressors, infections, irritants, and allergens. As the outermost layer of the skin, the stratum corneum (SC) contains a network of corneocytes embedded in a lipid matrix that provide the barrier function and protect against transepidermal water loss (TEWL). The lipid matrix in the SC contains lipids organized in a specific ratio: ceramides (40-50 percent), cholesterol (25 percent) and free fatty acids (10-15 percent). The corneocytes contain natural moisturizing factor (NMF), which is a collection of hygroscopic molecules including amino acids that retain water in the cells.

It is well established that a variety of external and internal factors lead to a decrease or disturbance of SC lipids, thereby increasing water loss from the SC and contributing to xerosis. External factors known to decrease SC lipids include certain chemicals, allergic contact dermatitis, irritant contact dermatitis, and climate extremes. Internal factors that decrease SC lipids include extremes of age, acute psychosocial stress, sleep deprivation, diet, as well as a variety of skin diseases. The prototypical disease associated with dry skin is atopic dermatitis (AD), but a variety of other conditions have decreased lipid levels, including psoriasis, acne vulgaris treated skin, and rosacea. The skin barrier is maintained, in part, by filaggrin, a key SC protein that influences a number of pathways, including maintenance of SC ceramides, and also contributes to the production of NMF. Filaggrin mutations have consistently shown to be associated with the development of AD.

In healthy skin, lipid homeostasis in the SC is maintained tightly. An insult to the SC barrier typically results in a cascade that quickly returns the proper type and amount of lipids to the epidermis to restore barrier function. However, in skin affected by various disease states, the ability of the SC to regenerate the appropriate amount of lipids is impaired and as such, a prolonged barrier dysfunction ensues.

To counter this barrier dysfunction, moisturizers have a long-standing history of use on diseased skin. Moisturizers, in the form of lotions, creams, or ointments, and sometimes even gels or foams, improve skin hydration, provide comfort, and decrease itch. Moisturizers can include humectants (e.g. urea, glycerol, lactic acid) that attract water to the SC and therefore compensate for reduced levels of NMF; occlusives (petrolatum, mineral oil, dimethicone) that form a layer on the skin surface and prevent TEWL; and emollients (lanolin, glycerol stearate, glyceryl stearate) that soften the skin and make it smoother. The terms “moisturizer” and “emollient” are often used interchangeably in the literature in a dermatologic example of metonymy. While it makes logical sense to include adjuvant ingredients, such as ceramides, fatty acids, urea and glycerol, in moisturizers, we are currently lacking strong evidence that these products truly improve moisturizer efficacy and need further research to confirm these suspicions.

CLASSIFYING MOISTURIZERS

Traditionally, moisturizers have been considered cosmetics and are sold in an relatively unregulated environment. However, it has recently been argued that moisturizers should be considered at least “cosmeceuticals” if not true pharmaceuticals, and covered under prescription drug insurance since they have the ability to modify functioning of skin and are considered first-line therapy for all dry-skin conditions. This is further supported by the fact...
that patients with dry-skin conditions are likely to require large quantities of moisturizers that are to be applied several times per day, sometimes totaling 250-500g/week. As moisturizers are not currently covered by most plans, this treatment modality can impose a significant financial burden on patients and their families, with one recent study estimating families with a child with AD spend an average of $28 per month on over-the-counter (OTC) products.

Not all moisturizers are identical, of course, and the selection of a specific moisturizer for by a patient is generally guided by disease type, disease severity, and patient preferences. As our understanding of various dry-skin skin conditions evolves, we can begin to better match disease pathology with appropriate moisturizers.

Thus, it is increasingly important to have an understanding of the evidence for the use of specific moisturizers for certain skin conditions. Since AD is the hallmark condition associated with dry skin and studies have demonstrated that use of moisturizers results in improved control of AD and a decreased need for topical corticosteroids (TCS), significant research has been done on the use of moisturizers in AD. In a recent review article, Moncrieff et al. recommended the use of occlusive emollient creams with an oil-in-water emulsion as first line therapy for mild/moderate dry skin in AD, followed by the use of an occlusive emollient ointment with a water-in-oil emulsions for more severe AD and an occlusive ointment with no water, such as white soft paraffin or liquid paraffin, for patients with very severe eczema. While this is a compelling paradigm, experience dictates that this will not be suitable for all patients, and evidence is lacking that outcomes would be improved with such an approach. Put bluntly, there are many patients with severe AD who abhor greasy preparations and simply will not use them, while many patients with milder disease find that creams can sting and burn, and will only use greasy ointments. Such cosmetic and practical considerations undermine a strictly scientific approach to this area.

Natural oils also have a role in treating the skin barrier observed in AD. However, it is important to note that not all natural oils are beneficial or safe, making critical evaluation of oils essential. Oils high in the unsaturated linoleic acid likely enhance barrier function while oils high in oleic acid enhance penetration through the SC. Sunflower seed oil (SSO) has demonstrated effectiveness in improving SC barrier function and skin hydration, which may be beneficial in the prevention and treatment of AD, effects that are likely mediated by the high linoleic acid content of SSO. Coconut oil has also been shown to improve the skin barrier, and has additional anti-inflammatory and anti-microbial properties, likely due to the presence of medium-chain fatty acids. On the other hand, olive oil, which contains high oleic acid content, results in impaired SC integrity, does not improve SC hydration and induces erythema for patients with AD, and as such, should probably be avoided.

ADDITIVES AND SAFETY

Given the high quantity of moisturizers required to treat AD and other dry-skin conditions, the scientific community and public have raised concerns about the safety of certain additives in moisturizer, specifically parabens. Parabens are preservatives used to protect against bacteria, fungi, and yeast in a wide range of cosmetic, pharmaceutical, and some food products. The potential estrogenic activity of parabens has prompted investigation of their role in breast cancer development. While parabens do bind estrogen receptors, the affinity of parabens is 10,000 to 1,000,000 times less than estradiol. A 2004 study by Darbre et al. detected the presence of parabens in the breast tissue of patients with breast cancer, sparking significant controversy about their use. However, the results from the Darbre study were called into question as no control tissues were examined and the authors did not comment on history of chemotherapy use, which may contain parabens, thus calling into the question their claim of causality.

Furthermore, studies investigating the link between underarm antiperspirants containing parabens and breast cancer risk show no increased cancer risk. Parabens have been used since the 1930s and have been shown to be rapidly absorbed, metabolized, and excreted. Paraben-containing products do seem safe but preservative-free products are available for patients who wish to avoid parabens. In particular, paraben-free products may be useful for patients with damaged or broken skin, such as AD patients, since patients with broken skin are at risk for sensitization from parabens. Excitingly, some skin care products have...
CLINICAL FOCUS

70
PRACTICAL DERMATOLOGY
JUNE 2017

Successfully avoided preservatives altogether by implementing airtight technology for packaging.

MOISTURIZERS BEYOND AD

Looking at moisturizers for dry-skin conditions beyond AD, patients with psoriasis benefit from moisturizers as they normalize hyperproliferation, differentiation, and apoptosis. Moisturizers also exert anti-inflammatory effects, improve barrier function, and enhance stratum corneum hydration. Moncrieff et al. recommended humectant-containing emollients, such as glycerin and urea, be used as first line moisturizers for patients with psoriasis.

Interestingly, it is now known that acne vulgaris (AV) may be due in part to skin barrier dysfunction. In acne-affected skin, barrier function is impaired, resulting in decreased moisture and ceramides. A recent review suggests that moisturizers can improve skin dryness and irritation for patients with AV and that ceramide-containing moisturizers may enhance adherence and complement existing acne therapies.

It is important that moisturizers for patients with AV be non-comedogenic. Evaluation of the comedogenicity of facial products was originally done with a rabbit external ear canal assay that measured the level of microcomedones and comedogenic grades were established on a scale of 0 (no comedogenic potential) to 3 (severe comedogenic potential). For the past 20 years, human models of comedogenicity have been developed and used, where test materials are applied under occlusion to the back for four weeks. However, the challenge associated with any model of comedogenicity is that the final analysis is affected by the number of applications, the timing of applications, amount applied, duration of application, method of response evaluation, and evaluation scale. An original report in 1996 found petrolatum has no comedogenic potential and concluded that greasiness cannot be equated with comedogenicity, however, no further evaluation with newer comedogenicity assay has been done on petrolatum, which is a key moisturizer for a variety of dry-skin related conditions. Today, studies employ a variety of comedogenic assays and most manufacturers combine comedogenicity testing with clinical use tests (individuals use the product under normal conditions for several weeks), leading to some ambiguity around the exact definition of “non-comedogenic.”

Finally, rosacea is also associated with an impaired SC, and moisturizers are recommended routinely for rosacea patients. Barrier defects occur in both clinically affected and normal-appearing facial skin. Barrier repairing moisturizers may assist in decreasing rosacea flares and reduce dryness and sensitivity. Recommended moisturizers include those that have: an acidic-neutral pH to minimize the flux in skin pH; surfactants or emulsifiers that will not strip the skin of its moisture or strip the lipids and proteins of the stratum corneum; and moisturizing ingredients such as emollients, humectants, and occlusive. Again, however, no specific moisturizer has been shown to be superior in rosacea, as with other disease states.

PRESCRIPTION EMOLLIENT DEVICES: A CLOSER LOOK

Prescription emollient devices (PED) have recently been developed to target specific aspects of skin barrier dysfunction and are approved for a variety of dry-skin conditions. PED are considered medical devices (as opposed to drugs) by the FDA that require 510(k) approval since they are believed to induce a physical change in the skin, specifically a decrease in the TEWL. However the approval process for PED focuses on safety rather than efficacy. These products are intended to provide physiologic lipid replacement therapy, particularly ceramides, to restore the normal balance of the epidermal barrier. PED are speculated to act by penetrating the SC, be synthesized into the keratinocyte and then be secreted back into the SC. Formulations vary depending on ratio of lipids and ability to penetrate into deeper layers of the skin by using systems such as a...


