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## The Importance of Quality Skincare for Barrier Repair During Acne Therapy

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## Abstract

Acne is a common chronic inflammatory disorder with multifactorial pathophysiology. One factor, impaired barrier function, has until recently been underappreciated. Data shows that acne-prone skin displays an inherent barrier deficiency highlighted by increased transepidermal water loss and substantive abnormalities in stratum corneum proteins and lipids. Acne therapy often involves exfoliants and irritants such as hydroxy acids, benzoyl peroxide, and retinoids that can exacerbate the barrier dysfunction.

The clinician's role in acne care is to devise a treatment regimen that is tailored to the individual patient, including topical and oral medications to address the underlying pathogenesis of acne. They also play a crucial role in recommending appropriate adjunctive nonprescription therapy. Over-the-counter products aid in acne therapy in numerous ways: lesion reduction, repair of the inherent barrier dysfunction, and maintenance of stratum corneum health during prescription treatment.

Barrier repair reduces the symptoms of irritation, which often lead to nonadherent medication behavior and subsequent reduced efficacy. This review is intended to provide a primer on skin care in acne and to highlight evidence-based advances in cleansers and moisturizers that serve as cornerstones for optimized acne therapy.

## Introduction

Acne is a common multifactorial inflammatory skin condition affecting up to 50 million Americans.<sup>1</sup> Traditional tenets of acne pathophysiology have indicated four central factors: hyper- and dysseborrhea, *Cutibacterium acnes* colonization, hyperkeratinization, and inflammation. More recently, studies have implicated the role of skin barrier dysfunction as a material contributor to the pathophysiology of acne. There is altered expression of barrier molecules, including filaggrin, involucrin, keratin, desmoglein, and aquaporin-3, proteins that regulate cohesion, desquamation, and hydration, resulting in compromised barrier integrity.<sup>2,3</sup> Increased transepidermal water loss (TEWL), increased pH, decreased microbial diversity, and decreased ceramide levels have been demonstrated, with the extent of the abnormality directly proportional to the severity of disease.<sup>4,5</sup> This leads to skin dryness, irritation, and increased sensitivity.<sup>6</sup>

Combined, these data suggest that the barrier function of acne-prone skin is inherently abnormal at baseline. Barrier dysfunction is accompanied by hyperkeratosis of the follicular epithelium, and Yamamoto and others have posited that this could promote comedone formation.<sup>4,7,8</sup>

In addition to the inherent barrier dysfunction, the use of topical medications and over-the-counter (OTC) acne products often results in side effects of skin dryness and irritation as a consequence of their keratolytic, sebostatic, and bacteriocidal activities.<sup>7,9-15</sup> Benzoyl peroxide has been shown to damage the barrier and disrupt the microbiome in a concentration- and vehicle-dependent manner; increased sebum levels, increased TEWL, decreased hydration, and decreased microbial diversity are the consequences of its use.<sup>16</sup> Topical retinoids and chemical peels also disrupt the barrier and may temporarily strip the microbiome.

Harsh cleansers are often chosen by uninformed oily acne patients due to their antimicrobial claims. They contribute to barrier dysfunction by further stripping natural moisturizing factor (NMF) compounds and lamellar lipids. Together, the net result is the exacerbation of the inherent barrier deficiency, which affects compliance with therapy.<sup>17-22</sup>

Acne treatment guidelines recommend that the acne management paradigm be built upon a foundation of benzoyl peroxide and a retinoid.<sup>23</sup> Studies and expert consensus have concluded that the use of gentle cleansers and quality moisturizers can minimize the adverse events of dryness and irritation.<sup>7,24,25</sup> Adherence to acne regimens, particularly in the teenage population, is notoriously poor, and iatrogenic skin irritation is a common factor leading to that nonadherent behavior.<sup>17,26,27</sup> Specifically, side effects of stinging, burning, redness, and dryness were found to be major reasons for nonadherent behavior.<sup>28-31</sup> Adding moisturizers to medication regimens improves adherence by decreasing side effects and improving acne lesion count.<sup>15,20,21</sup> Feldman and Chen also noted that irritation resulted in an increase in office complaint call-backs

and loss of faith in the provider.<sup>22</sup> Ultimately, improved adherence resulting from good skin care allows for maximum treatment outcomes.<sup>7,13,33-35</sup>

## Baseline Stratum Corneum Deficiencies in Acne-Prone Skin

Acne is associated with a decrease in filaggrin<sup>2</sup> and aquaporin-3 proteins.<sup>3</sup> These epidermal proteins are necessary to sustain stratum corneum hydration and barrier function. Filaggrin breaks down into NMF in the corneocytes<sup>36-38</sup> and aquaporins transport water from the viable layers of the epidermis to the stratum corneum.<sup>3,39,40</sup> Deficiency in either protein results in decreased water-holding capacity of the stratum corneum and overall dysfunction.<sup>3,39,40</sup> Stratum corneum hydration is critical for the delicate balance of enzymes responsible for desquamation.<sup>41-44</sup> Under low moisture circumstances, there is an accumulation of nonviable cells that may occlude the follicle leading to acne.<sup>45,46</sup> The overall goal of skin care is to use cleansers that do not worsen the baseline abnormalities by stripping still more filaggrin and lipids, and moisturizers that hydrate the skin and replenish the missing components.

## Cleansing

It is generally understood that cleansing is an important part of skin hygiene, removing dirt, oil, microorganisms, and allergens. However, cleansing with harsh surfactants can cause more harm than good by removing essential lipids, natural moisturizing factors, and beneficial microorganisms. Particularly in acne patients, it is important not to disturb the barrier any further than baseline, as this can worsen acne and decrease the patient's ability to use beneficial medications. It is useful in this regard to consider acne-prone skin to be analogous to clinically diagnosed sensitive skin and to make choices accordingly. Surfactant choice, pH, and patient preference figure into our decisions.

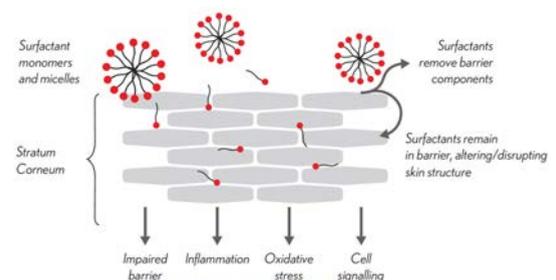
All cleansers rely on surfactants to remove dirt and oil. Surfactants are amphiphilic molecules with a hydrophilic head and hydrophobic tail (Figure 1).

Figure 1. Surfactant structure.



In water, they tend to assemble into micelles and bind impurities within, while the outward-facing hydrophilic heads allow the entire assembly to be rinsed off with water. Surfactant charge (neutral, anionic, cationic, amphoteric) and micelle formation determine both the mildness of the cleanser and its foaming action. When alkaline detergents are used, free surfactant monomers are able to penetrate the skin where they interact with proteins and lipids, causing the sensation of skin tightness and the outcome of irritation and itch (Figure 2).

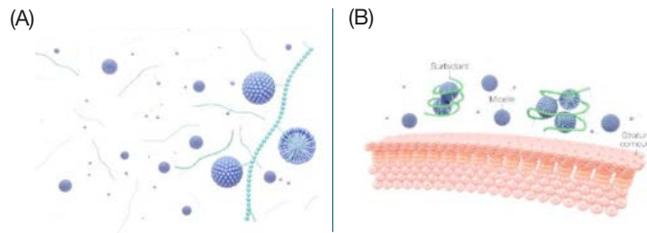
Figure 2. Damaging effects of harsh surfactants.



Adapted from Walters RM, *Derm Res Pract.* 2012.495917

Polymeric surfactant cleansing technology (PCT) is one method by which micelle penetration can be limited. It strikes a balance between effective cleansing and foaming while minimizing irritation. Hydrophobically modified polymers such as potassium acrylate copolymer interact with the hydrophobic tails of the surfactant, creating large micelles that fail to penetrate the stratum corneum; there is also a decrease in the concentration of free surfactant monomers (Figure 3A). This allows for the use of increased cleanser concentrations that promote higher quality foaming ability. The use of sodium hydrolysed potato starch dodeceny succinate (SHPSD) in addition to PCT or as a standalone creates even larger complexes that create rich foam without irritation (Figure 3B). Biodegradability is an additional benefit. Although rich foam is not a required component for an effective cleanser, most patients, especially oily-skin acne patients, prefer cleansers that lather well.

Figure 3. (A) Binding of micelles by hydrophobically modified polymer (B) Additional binding of potato-starch surfactant to increase micelle size.



Cleanser pH is an important characteristic to consider. The physiologic pH of the skin is acidic: between 4 and 6. Within this range, the stratum corneum functions to its highest capacity. Enzymes associated with differentiation and desquamation are optimized, the microbiome is more physiologic and there is a decrease in inflammation.<sup>13,47</sup> The pH of acne-prone skin is higher at baseline, making skin more prone to irritation from medications.<sup>48</sup> Quality cleansers with low pH can normalize the pH, thus improving barrier function and decreasing inflammation.<sup>8,27,49,50</sup>

A Hydrating Gel Cleanser uses PCT in combination with SHPSD, producing large micelles, less irritation, and superior foaming ability. In a study of 85 subjects with sensitive skin, including acne, use of the cleanser resulted in the absence of increased TEWL, no change in pH, and a statistically significant reduction in overall skin appearance and symptoms of stinging, itching, burning, and tightness after 2 and 4 weeks of daily use.<sup>51</sup> There was also no change in the microbiome, NMF levels, or lipid markers, indicating the absence of skin stripping. It is worth noting that it is unusual to see *improvements* in skin appearance, such as softness and smoothness, following the use of a cleanser – these are qualities that are normally attributed to moisturizers. It is a testament to the gentleness of the polymer cleansing technology that such a result is possible without additional products.

Another cleanser specifically intended for acne-prone skin uses the SHPSD combined with a novel salicylic acid formulation. Conventional salicylic acid has low water solubility, which limits its permeability and therefore efficacy when used topically. Additionally, when combined with foaming surfactants, salicylic acid is often drying. Overall, conventional salicylic acid cleansers can result in irritation without displaying significant efficacy against acne. A novel 2% salicylic acid cleanser uses a microgel complex that contains cetyl lactate and alkyl lactate that dissolve sebum, allowing the salicylic acid to penetrate deeper into the follicle<sup>52</sup> (Figure 4). The addition of SHPSD increased the aesthetically pleasing foaming capacity of the cleanser without causing irritation. In a study of 35 subjects over 12 weeks of daily use, 33.7% saw a decrease in total lesion count.<sup>52</sup> This was accompanied by a statistically significant improvement in overall appearance. There was no change in ceramides, cholesterol, or free fatty acid, indicating no disruption in barrier lipids.<sup>52</sup>

**Moisturizers**

Quality moisturizers that restore and maintain barrier function have numerous characteristics (Table 1). Humectants are hygroscopic

Figure 4. Microgel complex increases salicylic acid (red) in pilosebaceous unit compared to conventional salicylic acid.

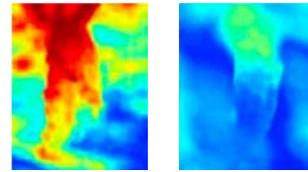


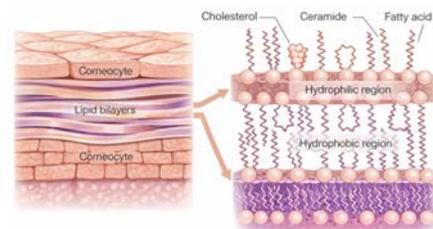
TABLE 1. Considerations for Moisturizer Ingredients for Acne-Prone Skin

	Purpose	Example Ingredients
Humectants	Attract and bind water	Glycerin, hyaluronic acid, NMFs (urea, amino acids, electrolytes, lactate, PCA)
Occlusives	Skin protective, decreased TEWL	Petrolatum, silicones, lanolin, mineral oil
Emollients	Smooth skin	Cetyl alcohol, steryl alcohol, plant oils (sunflower, safflower, avocado, coconut)
Physiologic lipids	Repair and support of lipid bilayer, decreased TEWL	Ceramides, cholesterol, free fatty acids
Cosmeceuticals	Anti-inflammatory, anti-oxidant, occlusive	Allantoin, panthenol, niacinamide, vitamin E, linoleic acid, <i>Centella asiatica</i> , probiotics

NMF: Natural moisturizing factor, PCA: Pyrrolidone carboxylic acid, TEWL: Transepidermal water loss

molecules that attract and bind water, increasing stratum corneum hydration. Common humectants include NMFs, glycerin, and hyaluronic acid. Occlusives provide a barrier to prevent water loss and to protect the skin surface from pathogens and allergens. Petrolatum, silicones, lanolin, and mineral oil all function to seal moisture within the stratum corneum. Emollients such as cetyl and steryl alcohol, as well as plant oils, serve to smooth the skin. Physiologic lipids such as ceramides, cholesterol, and free fatty acids together in equimolar concentrations comprise the lipid bilayer (Figure 5). Topically applied, they are incorporated into the lipid bilayer, augmenting and/or replacing missing or dysfunctional ingredients in diseased skin. Cosmeceuticals (agents that are at the juncture of cosmetics and drugs) are often added to moisturizers to augment the occlusive or humectant qualities of the product, as well as adding soothing, anti-inflammatory, and antioxidant qualities.

Figure 5. Healthy lipid bilayer structure.



**Importance of the Skin Microbiome in Barrier Health**

The skin barrier comprises physical, chemical, and microbial components that function together to maximize skin health. The stratum corneum and microbiome have a mutualistic relationship. The skin provides a niche in which live moisture and food. The microbiome, in turn, occupies the niche and consumes the nutrients that might otherwise be taken/consumed by pathogens, acidifies the stratum corneum, making it less hospitable to pathogens like *S. aureus*, and aids in host defense and innate immunity. Changes in either barrier composition or microbial communities impact the other. In acne, both systems are often disrupted. As mentioned previously, innate barrier dysfunction is a hallmark of acne-prone skin. The use of topical retinoids, benzoyl peroxide, hydroxy acids, and isotretinoin are all associated with barrier disruption, decreased hydration, and increased TEWL. Additionally, topical and oral antibiotics, as well as isotretinoin, alter the cutaneous microbiome. These changes may contribute to increased inflammation and iatrogenic irritation, as well

as reduced treatment adherence, resulting in decreased therapeutic efficacy. Moisturizers are necessary to enhance hydration, replenish intercellular lipids, and help to stabilize the microbiome. As such, moisturizers function as prebiotics, and postbiotics like succinic acid can also be incorporated to promote microbiome health.

### Moisturizers for Acne-Prone Skin

Traditional moisturizers that are intended to reduce skin sensitivity and irritation contain large amounts of occlusives and emollients that may be counterproductive for acne-prone skin. These ingredients are often comedogenic and leave unpleasant greasy residues that acne patients find particularly unpleasant, leading to poor compliance. Acne patients often have a combination of excess sebum with acne-related and medication-related dryness and need to be reminded that sebum is not a moisturizer. What is needed for acne patients is a lightweight moisturizer that provides hydration without a greasy residue, does not clog pores, is nonirritating to sensitive acne-prone skin, and helps to combat iatrogenic irritation.

A gel-matrix moisturizer (Hydroboost® Gel Cream Moisturizer) and a water-cream moisturizer (Hydroboost® Water Cream Moisturizer) have been studied in acne patients.<sup>53,54</sup> Both products contain NMF components (amino acids, electrolytes, urea, PCA, lactate) as well as glycerin and hyaluronic acid as humectants to attract and bind water, dimethicone as an occlusive, and cetyl alcohol as an emollient. Additionally, the water cream contains physiologic lipids: ceramides, cholesterol, and free fatty acids. Both products are lightweight and residue-free with the water-cream having a richer texture due to the physiological lipids.

Both products were evaluated in preclinical and clinical studies.<sup>53,54</sup> Skin explants were used for the preclinical studies that showed, after 2-3 days, an upregulation of genes involved in synthesis, metabolism, and exportation of lipid precursors, an increase in the levels of filaggrin, aquaporin-3, hyaluronic acid, and neutral lipids. These findings indicate that the products are not just adding moisture to the skin; they are triggering epidermal repair from within. Clinically, after 4 weeks of once to twice daily use, there was a decrease in TEWL and an increase in hydration, which persisted during a 3-day regression. There was a significant improvement in all parameters of skin health, including erythema, peeling, flaking, drying, itch, tightness, and overall skin sensitivity. Patients who were concomitantly on acne medications noted an increase in compliance with their prescribed products.

### Conclusion

Skin barrier repair and maintenance in acne serves two distinct purposes: repair of baseline barrier dysfunction and improved medication adherence with optimized efficacy. Due to the innate barrier dysfunction in acne-prone skin, maximizing barrier and microbiome health may alone result in acne improvement. Small studies have demonstrated that quality skincare can reduce TEWL, acidify the skin pH, and foster the growth of a healthy microbiome.<sup>55</sup> This may offer an explanation for the unexpectedly positive results seen in the vehicle arms of recent phase 3 acne studies; improved vehicle technology, as well as dispensing quality skin care for study subjects, may augment the efficacy of the active ingredient. Second, the use of appropriate skin care to improve pharmacologic tolerability and adherence is associated with superior clinical outcomes.

A holistic approach to all dermatologic conditions, including cleansing, moisturization, and sun protection in addition to prescription therapy is recognized as essential to skin health. Patient education regarding the importance of adjunctive therapy is crucial to ensure the use of quality products and the avoidance of potentially harmful agents touted in internet fads. However, time constraints in a busy office often means that skincare takes a back seat. Additionally, it is important to tailor product recommendations to the individual patient. Considerations include the severity of the acne, patient preference for aesthetic qualities of cleansers and moisturizers, and consequential adherence. Also important in the decision-making process is anticipating the irritation potential of the

topical acne products being prescribed. Recent advances in vehicle technology have provided clinicians with superior products with improved tolerability. Unfortunately, affordability is often a deterrent to accessing such medications. Quality cleansers and moisturizers that help to restore and maintain barrier function are crucial for such patients.

A comprehensive approach to acne care must incorporate adjunctive skincare with careful attention to ingredient and formulation selection and patient preference that aid clinicians in optimizing clinical results. Given the expansive selection of commercial cleansers and moisturizers and excessive internet noise, it is important to combat patient choice paralysis by providing specific brand-name recommendations and use instructions.

### Disclosure

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