

# Skin Care Based on Science: Improving Outcomes in Rosacea

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Patients with rosacea have compromised skin barrier function and are more prone to dryness, irritation, and skin sensitivity. With an understanding of the pathogenesis and inherent skin problems that rosacea patients experience, it is essential for dermatologists to provide specific recommendations for skin care. Cleansers and moisturizers must be selected to improve skin barrier function and reduce inflammation. Cosmeceuticals with anti-inflammatory actives may be helpful in mitigating the signs and symptoms of rosacea. This article will review topical skin care products that may improve treatment outcomes in rosacea patients.

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Rosacea patients are a unique challenge for dermatologists, often reporting stinging, burning, and exacerbation of disease symptoms after using topical skin care products. Patients with rosacea have compromised skin barrier function and are more prone to irritation and inflammation. Thus proper product selection is of utmost importance in this patient population. This article will review cleansers, moisturizers, and cosmeceuticals that may improve treatment outcomes in rosacea patients.

## BACKGROUND

Affecting an estimated 14 million Americans, rosacea is one of the most common conditions treated by dermatologists.<sup>1</sup> As defined by the National Rosacea Society Expert Committee on the Classification and Staging of Rosacea,<sup>2</sup> there are 4 subtypes of rosacea, the most

common being erythematotelangiectatic rosacea (ETR), which presents as diffuse macular erythema of the central face. Flushing is common in ETR and occurs without provocation or in response to triggers such as heat, exercise, hot spicy foods, and alcohol. Telangiectasia can be severe in more advanced cases and is a prominent cosmetic problem. The second most common subtype is papulopustular rosacea (PPR), which can be confused with acne because it is characterized by inflammatory papules and pustules on the central face; however, the lack of comedones and presence of a background of diffuse macular erythema help to differentiate PPR from acne. Phymatous and ocular rosacea are less common subtypes and are among the most difficult to treat.<sup>2</sup> This article will primarily focus on the skin care needs of patients with ETR and PPR.

Our knowledge of the pathogenesis of rosacea has substantially increased in recent years.<sup>3-6</sup> Rosacea is an inflammatory condition that is triggered by immune dysfunction.<sup>4</sup> Immune peptides known as cathelicidins are increased in the skin of patients with rosacea.<sup>5,6</sup> Cathelicidins are antimicrobial peptides that are angiogenic and chemotactic, attracting mast cells other inflammatory cells. Cathelicidins generate reactive oxygen species that also have been implicated in rosacea.<sup>7</sup> It has been proposed that antigens from bacteria that reside within

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*Demodex folliculorum* may trigger these antimicrobial peptides.<sup>8</sup> Studies on the role of *Demodex* in the pathogenesis of rosacea are ongoing.

Rosacea is characterized by an impaired epidermal barrier function, resulting in an increase in transepidermal water loss (TEWL) in clinically involved skin.<sup>9</sup> Rosacea patients often report burning and stinging when applying skin care products and are highly susceptible to irritation. It is believed that the barrier defect caused by rosacea allows potential irritants to reach deeper layers of the epidermis and dermis, causing sensations of stinging and burning. When tested with the lactic acid stinging test for skin sensitivity, 100% (7/7) of patients with ETR and 68% (17/25) of patients with PPR had stinging compared with 19% (6/32) of controls.<sup>10</sup> Contact and irritant dermatitis also are seen more frequently in patients with rosacea.<sup>11</sup>

With an understanding of the pathogenesis and inherent skin problems that rosacea patients experience, it is essential for dermatologists to provide specific recommendations for skin care. Regimens must include cleansers and moisturizers that will not exacerbate signs and symptoms of rosacea but instead will improve epidermal barrier function and reduce inflammation. Cosmeceuticals containing anti-inflammatory actives also may be helpful in mitigating the signs and symptoms of rosacea.

## SOAPS AND CLEANSERS

Choosing facial cleansers for rosacea patients requires a basic understanding of the products that are commercially available as well as factors that contribute to irritancy. All cleansers are designed to remove dirt, environmental pollutants, sweat, and sebum using surfactants. Surfactants are classified according to their charge or lack of charge as anionic, cationic, nonionic, or amphoteric (having both positive and negative charges).<sup>12,13</sup> Harsh surfactants can damage proteins and disrupt lipids in the stratum corneum, contributing to epidermal barrier dysfunction.<sup>14-16</sup> Anionic and cationic surfactants generally are more irritating than nonionic and amphoteric surfactants.<sup>12</sup> Because anionic surfactants are among the most effective, modern cleansing formulations use small amounts of anionic surfactants in combination with milder surfactants to reduce irritation.

Hydrogen ion concentration (pH) is another important factor that contributes to the irritancy of a cleanser. Under normal circumstances, the pH of the skin is slightly acidic with an average of 4.7 (range, 4.5–6.5).<sup>17</sup> Continued use of alkaline soaps or cleansers will increase the pH of skin, causing functional changes such as disrupted skin lipids, altered bacterial flora, and compromised skin barrier function.<sup>18-20</sup> Thus using a cleanser with an

inherently neutral or slightly acidic pH is preferable for patients with rosacea.

True soaps are created by saponification through which long-chain fatty acids are combined with an alkali, resulting in fatty acid salts.<sup>21</sup> True soaps are basic with a pH of 9 to 10, which is far greater than the skin's pH.<sup>18,19</sup> Combination bars (combars) are a combination of true soap and synthetic detergents; they may contain antibacterial agents such as triclosan.<sup>22</sup> Combars are alkaline (pH of 9–10) and contain antibacterial ingredients that can cause irritation, making them a poor choice for patients with rosacea.<sup>21,22</sup>

Milder cleansing alternatives include synthetic detergent bars (syndets) and lipid-free cleansers. Syndets are comprised of synthetic detergents and contain less than 10% soap<sup>14,21,22</sup>; they also have a more favorable pH (5.5–7) and provide excellent cleansing with less irritation than true soaps or combars.<sup>19,21</sup> Syndet liquid cleansers have similar properties to syndet bars. Most gentle bar soaps that are available today are syndet-type products. Lipid-free cleansers are gentle and have unique properties.<sup>21-23</sup> They cleanse without any fat and have a neutral or slightly acidic pH. Lipid-free liquid cleansers are effective in cleansing the face and removing makeup. These cleansers do not lather and are designed to leave a thin moisturizing film on the skin.

Table 1 lists mild facial cleansers for rosacea patients.

Studies have indicated that lipid-free cleansers and syndet bars have important advantages for patients with rosacea. In a randomized, double-blind study, rosacea patients used either a syndet bar (Dove Sensitive Skin Unscented Beauty Bar, Unilever) or an unnamed true soap in conjunction with metronidazole gel 0.75% (MetroGel, Galderma Laboratories, LP). At the end of the 4-week trial, it was noted that the soap worsened skin conditions, while the syndet bar improved dryness, irritation, and itching. Patients also preferred the syndet bar over true soap.<sup>15</sup>

Draelos<sup>23</sup> compared the use of a nonalkaline lipid-free cleanser (Cetaphil Gentle Skin Cleanser, Galderma Laboratories, LP) with a syndet bar (Dove Sensitive Skin Unscented Beauty Bar) in patients with PPR. Objective measures revealed a compromise in barrier function in patients using the syndet bar as demonstrated by an increase in TEWL and decrease in skin hydration after 2 weeks. Patients using the lipid-free cleanser showed a significant decrease in TEWL at week 1 ( $P < .05$ ) that returned to baseline after 2 weeks. There also was a significant drop in rosacea severity score in patients using the lipid-free cleanser ( $P < .001$ ), and patients preferred the lipid-free cleanser to the syndet bar.<sup>23</sup>

In addition to cleanser recommendations, dermatologists also can offer helpful instructions for rosacea patients to minimize flare-ups that can occur from improper washing. Hot water causes vasodilation and can trigger flushing, thus exacerbating facial redness. Excessive mechanical stimulation of the skin also should be avoided. Woven mesh sponges and abrasive brushes designed to exfoliate the skin are not recommended for patients with rosacea; use of a gentle open-weave cloth or the fingertips is a gentler alternative. Granular scrubs are abrasive and can be irritating. Soft rotating brushes are popular with consumers and are viewed as a gentle alternative to washcloths; these devices may be used if the brush is soft and excessive pressure is not applied to the skin.

**ASTRINGENTS AND TONERS**

Astringents and toners are applied after cleansing to remove any residual oils remaining on the skin after the

cleansing process. Originally designed to remove soap residue, these products are now primarily used to remove oils left behind by cleansing creams and lipid-free cleansers.<sup>24</sup> Astringents and toners should not be used by rosacea patients because oils left behind from the cleansing process should not be removed. Additionally, astringents and toners rapidly evaporate from the skin, causing stinging, burning, and exacerbation of facial redness.<sup>24</sup>

**MOISTURIZERS**

The use of properly formulated moisturizers is important in the management of patients with rosacea.<sup>21</sup> Moisturizers help to mitigate dryness, improve barrier function, and reduce symptoms of skin sensitivity in patients with rosacea (Table 2).<sup>25-31</sup> In general, moisturizers contain 3 main components: occlusives, humectants, and emollients.<sup>32-34</sup>

Occlusive ingredients are oily substances that prevent water loss from the stratum corneum by forming an occlusive layer on the surface of the skin.<sup>32-34</sup> In essence, occlusive agents seal in water so that it is not lost to the environment, thus improving skin hydration. There are a wide range of occlusive ingredients used in moisturizers, though formulators prefer ingredients that have no odor and do not have a greasy feeling. Common occlusive ingredients include petrolatum, lanolin and lanolin alcohols, mineral oil, dimethicone, soybean oil, squalene, propylene glycol, lecithin, and ceramides.<sup>32-34</sup> Occlusive ingredients are essential to any effective moisturizing formulation.

Humectants are designed to rehydrate the stratum corneum by attracting water from the dermis and lower epidermis.<sup>35</sup> When the humidity is greater than 70%, humectants can draw water from the environment, hydrating the skin from the outside in. Common

TABLE 1 Mild Facial Cleansers <sup>18,19,21,24,a</sup>	
Syndets and Syndet Liquids	Lipid-Free Cleansers
Aveeno Moisturizing Bar (Johnson & Johnson Consumer Companies, Inc)	Aquanil Cleansing Lotion (Person & Covey, Inc)
Cetaphil Gentle Cleansing Bar (Galderma Laboratories, LP)	CeraVe Hydrating Cleanser (Coria Laboratories, a division of Valeant Pharmaceuticals North America)
Dove Sensitive Skin Unscented Beauty Bar (Unilever)	Cetaphil Gentle Skin Cleanser (Galderma Laboratories, LP)
Olay Ultra Moisture Bar (Procter & Gamble)	

<sup>a</sup>Based on pH and composition.

TABLE 2 Benefits of Moisturization in the Treatment of Rosacea <sup>27-31</sup>
<ul style="list-style-type: none"> <li>• Promotes barrier repair</li> <li>• Improves skin hydration</li> <li>• Reduces clinical dryness</li> <li>• Mitigates stinging and burning</li> <li>• May reduce irritation from topical medications</li> </ul>

humectants include glycerin, hyaluronic acid, sodium lactate, urea, glycolic acid, propylene glycol, and honey.<sup>32-34</sup> Humectants must be used in combination with occlusive agents so that the water they attract into the stratum corneum will not evaporate into the environment.

Emollients are used to improve the aesthetics of a moisturizer. Emollient ingredients fill the spaces between desquamating keratinocytes, making the skin feel smooth after a moisturizer is applied.<sup>32-34</sup> Lanolin, isopropyl myristate, soy sterol, sunflower seed oil, glycerol stearate, and cetyl and stearyl alcohols are commonly used emollients in moisturizers.

Most moisturizing formulations contain these 3 essential components in combination with water, thickeners, and preservatives.<sup>32-34</sup>

Moisturizers are emulsions.<sup>24</sup> Lotions are oil-in-water emulsions, while creams are water-in-oil emulsions. Creams are thicker than lotions and may be beneficial for patients with rosacea who have dry skin. Patients with rosacea should choose bland moisturizers because ingredients such as urea, glycolic acid, and lactic acid may cause a burning sensation. Moisturizers containing botanical additives with anti-inflammatory properties may provide an added benefit and will be discussed in the section on cosmeceuticals.

In clinical practice, rosacea patients apply moisturizers in combination with medications. In a study using a modified Franz cell assay, the application of 3 moisturizing lotions before or after application of azelaic acid (AzA) gel 15% was found to have no effect on the absorption of AzA. The 3 moisturizing lotions included Cetaphil Moisturizing lotion (Cetaphil Moisturizing Cream, Galderma Laboratories, LP), Dove Lotion (Unilever), and CeraVe Moisturizing Lotion (Coria Laboratories, a division of Valeant Pharmaceuticals North America).<sup>27</sup>

When chosen properly, moisturizers also may help reduce irritation that accompanies the use of topical medications. A 12-week study of rosacea patients using AzA gel 15% demonstrated that a skin care regimen including a gluconolactone cleanser (NeoStrata Facial Cleanser, NeoStrata Company, Inc) and moisturizer (NeoStrata Ultra Moisturizing Face Cream, NeoStrata Company, Inc) was superior to a patient-selected skin care regimen.<sup>28</sup> Although the test regimen did not improve the efficacy of AzA gel 15%, there was an improvement in skin dryness, texture, smoothness, and overall condition when compared with the patient-selected regimen. Participants using the test regimen also noted a reduction in skin sensitivity.<sup>28</sup>

Similarly, in a 15-day, split-face study of 20 participants with rosacea who were using metronidazole gel 0.75% twice daily, the addition of a nonalkaline moisturizing cream (Cetaphil Moisturizing Cream) twice daily was

found to enhance barrier function, reduce TEWL, and reduce response to lactic acid stinging test. Skin dryness, roughness, and desquamation also were improved, and skin sensitivity was reduced with use of the nonalkaline moisturizing cream.<sup>29</sup>

More recently, a large study of 102 rosacea patients evaluated the ability of a ceramide-based moisturizing cream (CeraVe Moisturizing Cream, Coria Laboratories, a division of Valeant Pharmaceuticals North America) or a nonalkaline moisturizing cream (Cetaphil Moisturizing Cream) to reduce irritation from AzA gel 15%. This 7-day, split-face study confirmed that the use of both creams resulted in significant improvement in stinging, burning, itching, and tingling compared with using AzA gel alone ( $P = .015$ ).<sup>30</sup>

These studies indicate that moisturizers provide added benefits when used in combination with topical medications for rosacea. Effective moisturization encourages barrier repair and reduces signs and symptoms of rosacea.<sup>28-30</sup> It has been suggested that patients with acute flares of rosacea may benefit from using an appropriate skin care regimen, including a mild cleanser and moisturizer, for several days prior to initiating topical medications.<sup>31</sup> This pretreatment phase improves stratum corneum hydration and encourages barrier repair prior to the initiation of topical therapy.

## COSMECEUTICALS

Cosmeceuticals have become an important part of the therapeutic armamentarium for treating photodamage, scars, and cellulite. In recent years, there also has been a growing interest in cosmeceuticals that will improve facial redness. The vast majority of these products are moisturizers that contain anti-inflammatory actives designed to mitigate the signs and symptoms of rosacea (Table 3).

### Botanical Actives

The gold standard botanical for soothing inflamed skin is colloidal oatmeal. Commercially available colloidal oatmeal is a protein-starch complex that is mixed with emollients and acts as both a skin protectant and an anti-inflammatory agent.<sup>36</sup> It has been widely used to treat patients with eczema. When applied to the skin, colloidal oatmeal forms a barrier that reduces TEWL and improves barrier function.<sup>36</sup> Avenanthramides are polyphenolic compounds in oats that exhibit anti-inflammatory and anti-itch properties. These compounds downregulate nuclear factor  $\kappa$ B, thereby reducing the production of proinflammatory cytokines.<sup>37</sup> There are no formal clinical studies assessing the benefits of oatmeal-containing moisturizers in patients with rosacea, but the clinical properties of this botanical suggest it may be helpful.

TABLE 3

### Cosmeceutical Actives for the Treatment of Rosacea<sup>36-47</sup>

- Aloe vera
- Colloidal oatmeal
- Feverfew
- Grape seed extract
- Green tea
- Licorice extract
- Niacinamide
- Quercetin
- Turmeric
- Vitamin C

Licorice plants (*Glycyrrhiza glabra* and *Glycyrrhiza inflata*) have long been known for their medicinal value. Licochalcone A is isolated from the root of *G inflata* and has been shown to have anti-inflammatory and antioxidant properties.<sup>38</sup> Licorice extracts have been used to treat a variety of inflammatory skin conditions including eczema.<sup>39</sup> In a clinical study, patients with facial redness applied a moisturizer containing licochalcone A (Eucerin Redness Relief Daily Perfecting Lotion SPF 15, Beiersdorf, Inc) twice daily for 8 weeks.<sup>40</sup> Participants included patients with rosacea and other skin conditions causing facial redness. The lotion was well-tolerated and improved mean erythema scores and quality of life scores.<sup>40</sup>

Feverfew (*Tanacetum parthenium*) is a botanical member of the chrysanthemum family and has diverse biologic activity. Feverfew is an antioxidant and anti-inflammatory agent that inhibits cytokine release by downregulating nuclear factor  $\kappa$ B.<sup>41</sup> The use of feverfew in cosmeceuticals has been limited by the fact that extracts contain parthenolides that are potent skin sensitizers; however, parthenolide-free feverfew (feverfew PFE [purified feverfew extract]) was developed and marketed as an anti-inflammatory cosmeceutical for patients with sensitive

skin and facial redness (Aveeno Ultra-Calming Daily Moisturizer With SPF 15, Johnson & Johnson Consumer Companies, Inc). In a 3-week study, patients using a lotion with feverfew PFE twice daily saw substantial improvements in UV light–induced facial redness, blotchy redness, and facial irritation.<sup>42</sup>

There are many botanical actives, including grape seed extract, resveratrol, quercetin, chamomile, aloe vera, turmeric, green tea, and mushroom extract, that have anti-inflammatory properties.<sup>43</sup> The use of cosmeceuticals containing botanicals with anti-inflammatory activity has great potential in treating inflammatory skin disorders. It is an area of ongoing research and interest in the cosmetic arena.

### Vitamin-Based Cosmeceuticals

Vitamin-based cosmeceuticals often are proposed as an adjunct therapy for patients with rosacea. Niacinamide is well-known for its ability to improve barrier function.<sup>44</sup> Niacinamide increases lipids in the skin including ceramides and barrier proteins such as keratin, involucrin, and filaggrin.<sup>44,45</sup> In a randomized, investigator-blinded, controlled study, rosacea patients applied a facial moisturizer containing niacinamide (Olay Total Effects 7× Visible Anti-Aging Vitamin Complex Fragrance Free, Procter & Gamble) twice daily to the face and 1 forearm for 4 weeks.<sup>46</sup> Barrier function and skin hydration were improved on the treated forearm and face following use of the moisturizer containing niacinamide. Both the patients and investigator noted improvement in facial erythema, dryness, and scaling over the course of the study.<sup>46</sup>

Topical vitamin C also is a potent antioxidant and anti-inflammatory and is available in a variety of cosmeceutical formulations, including creams, lotions, and serums.<sup>47</sup> A recent study demonstrated the efficacy of a sodium L-ascorbyl-2-phosphate 5% lotion in the treatment of patients with acne.<sup>48</sup> Considering what is known about the clinical benefits of topical vitamin C, it also may have a role in treating inflammatory conditions such as rosacea.

### COMMENT

Rosacea patients require extra care and guidance when it comes to selecting a daily skin care regimen. Choosing the right products can facilitate barrier repair and reduce the signs and symptoms of rosacea. Cleansers, moisturizers, and cosmeceuticals should all play a role in designing therapeutic skin care regimens for this patient population. As dermatologists, we have a unique advantage because we understand the pathophysiology of rosacea and have a basic understanding of the skin care products that will improve it.

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## SKIN CARE IN ROSACEA PATIENTS

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